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WALTER REED, C. FINLAY, AND THEIR PREDECESSORS AROUND 1800

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In 1900/01, the U. S. Army Yellow Fever Commission, headed by Walter Reed, proved experimentally a) that the stegomyia fasciata, now called Aedes aegypti, was the vector and b) that the disease was not contagious (1). Heeding W. H. Welch's suggestion—born out of Fr. Loeffler's and P. Frosch's studies on the etiology of the foot and mouth disease (2)—the Commission also succeeded c) in narrowing the search for the etiological agent to the group of filtrable viruses (3).

The experiments underlying conclusions *sub* (a) and (b) were immediately repeated; the results were confirmed by Dr. Guiteras of the Sanitary Department of Havana (4), and, still in 1901, successful sanitary measures were instituted and carried out under Gorgas' direction. As to the subject *sub* (c), new research techniques had to be invented before the agent could be isolated and a vaccine produced.

Could the Yellow Fever Commission rightfully claim priority in all three respects? Was it necessary to wait with the sanitary measures up to 1901, or could they have been taken on the basis of intelligent reasoning before that time? Did the Yellow Fever Commission open a new line of scientific development?

* * *

According to the prevailing impression, prior to 1900 very little scientific work on yellow fever was done beyond the formulation of theories on the pathogenesis and beyond the refutation of unfounded claims concerning the causative agent.[1] As a rule no mention is made of any successful experimentation on yellow fever prior to 1900. Finlay, who had since 1881 propagated the role of the stegomyia fasciata, started on experiments in this very year, but apparently failed. Also Dr. Ruis, in Vera Cruz, experimenting in 1885 and 1887 on the man-stegomyia-man cycle, had failed (5).

In the XVIIIth and in the first half of the XIXth centuries, there was a great deal of confusion about every single item concerning yellow fever. It was an era of nebulous notions about the mode of transmission of many then known diseases. Conclusions were sometimes based on observations, more often they were derived from deliberations according to some scheme of " Either—Or," although such a dichotomy was senseless and both alternatives were immaterial.[2]

Although B. Rush in the 1790's realized the abundance of mosquitoes during at least one of the fever epidemics, he did not conceive of mosquitoes as vectors. Describing the Philadelphia epidemic of 1794, Rush (pp. 57-58) quoted Bruce's and Dr. Clark's observations that persons who lived and worked in smoky houses (i. e. houses without, or with inadequate, chimneys) escaped the disease (7). According to Rush's interpretation, the smoke had kept away the miasma, the exhalations from the gutters and stagnating ponds. It was known that smoke protects man from mosquitoes but to Rush and all the others they were a nuisance only, while the miasma was a disease causing reality.

In this period of confusion one would hardly expect to find valuable—still less, successful—attempts at clarification of such matters. Where such attempts occurred, they were obviously out of step with their time and therefore bound to be little appreciated and soon forgotten.

It is believed that the earliest lasting contributions in the field of yellow fever and malaria in America were made in 1848, when J. C. Nott (8) assigned to mosquitoes a role in yellow fever, and in 1854, when L. D. Beauperthuy (9) suggested the stegomyia fasciata as the mosquito in question. It was the very same species to which Finlay too, later turned (10). However, none of these three was first to conceive of insects as the intermediaries in spreading infectious disease. It was still

[1] G. M. Sternberg (5) disproved the role of the bacillus tetragenous febris flavae believed in by Finlay, and Reed and Carroll did the same with respect to the bacillus icterogenes Sanarelli (3).

[2] For information, *see* R. La Roche (16).

in Rush's life time that a learned physician in Baltimore, J. Crawford (11), in a long series of articles under the headings "Remarks on Quarantine, suggested by Dr. Caldwell's oration" and "Doctor Crawford's Theory . . .," rejected the theory of miasma and pronounced mosquitoes to be the source of malaria, yellow fever, and other diseases.

Crawford dealt with a great variety of problems, with the history and uselessness of quarantine, with the theory of Malthus, with epidemiological observations on Cyprus (speaking against contagion), with the topographical distribution of yellow fever in Baltimore, with peculiarities of some insects depositing their eggs in the bodies of other insects and the consequences of it etc. etc. He arrived at the theory of mosquitoes as vectors of malaria and yellow fever, reasoning per analogy.

> If we can once be satisfied that the cause of death, obvious in any one creature, must resemble the cause producing death in every other, we shall be enabled to form conclusions respecting our own fate, that will generally give satisfaction. If this reasoning is just, it of necessity follows, that as the plague of the caterpillars, pucerons, and of all the insect tribes, is the ichneumon, which deposits its eggs in their bodies or in places near to where they abide, which when hatched prey upon them, either wholly at once or by parts . . . so the plague, yellow and every other fever, and every other disease we experience, must be occasioned by eggs insinuated, without our knowledge, into our bodies, externally or internally, or from eggs planted near our habitations which, when hatched, in either case prey upon us by parts, one description giving a preference to one part, and another to another (*2*: 50-51).

There is no "active substance generated from animal corruption, and preserved in soft porous bodies" (*2*: 52), and directly propagated from person to person. "As to yellow fever, the plague of the country, neither agriculture, nor cleanliness have, I fear, had any share either in impeding, or the want of them, in producing the dreadful scourge" (*2*: 66). This was directed against the miasma theory as professed by Rush and his pupils.

Thinking of yellow fever, it is difficult to build a bridge between Crawford's transmission of infection by insects and the role assigned at present to mosquitoes as carriers. Whether they infected by stinging, as some did, or by depositing material on the surface of the human body, as others did, it was, according to Crawford, always their own eggs—for the naked eye invisible or hardly visible—and the larvae which produced the disease, and the symptomatology depended on the insect's family or species. There is, however, one passage which indicates that in August 1807 Crawford may have come closer to the modern concept. To combat epidemics he had a two point program: "To prevent the non-infected

(*scil.* persons) from visiting the sources of infection, and to remove those that are infected from the vicinity wherein the evil abounds" (*2*: 69). The first requirement is logical, as according to the theory the evil abounds where the insects breed and "herd together," and whence they attack human beings to deposit eggs on or into them. If only the insect's egg counts, the second demand is illogical and unjustified. If, however, the patient is the source of infection for the insect which later transmits to other men the disease's cause via egg or larva (man-insect-man cycle), then the second point in Crawford's program is a logical necessity. Did he make this second step? I can not solve the dilemma.

Crawford attributed to insects too large a role in the genesis of human suffering and misinterpreted the mechanism by which they transmit yellow fever, but he was the first to turn from the hazy concepts of miasma and contagium to a tangible intermediate carrier, the insect. It is perhaps not easy for us to grasp the boldness of thought required for this step in the years 1790-1807, and the courage needed to pronounce and to propagate such strange ideas in spite of the vehement opposition of the whole profession. Crawford knew the award due to non-conformists; they are "villified, cruelly prosecuted or sunk into neglect" (*2*: 250). He was ridiculed and eventually lost his practice.

Finlay was the first to put the theory of transmission of yellow fever by the stegomyia to an experimental test, starting in June 1881. He claimed that of 90 inoculations of man by means of mosquito bites, 18% yielded positive results. However, all patients were but mildly sick, some with albuminuria, others without, and none was a typical case (12).

W. Reed and his associates refused to accept Finlay's diagnosis in these experimental cases, and refuted his claim on the following grounds:

Finlay's inoculations were made with mosquitoes contaminated only 2-6 days previously. Mosquitoes digest the blood within 2 to 3 days, whereupon they are ready for the next meal. Thus, 2 to 6 days after contamination they were ready to drink, but, according to the U. S. Army Yellow Fever Commission, were not yet abie to transmit the disease by stinging before 11 days after contamination were over (1). (Of eight non-immune men bitten by mosquitoes contaminated less than 12 days before, *all* remained healthy.) The 12th day marked the border between the probability of failure and success.

Finlay was ignorant of the long "maturation period" of the virus in the stegomyia and disagreed with the Commission's argumentation (13). Had the latter been right in this respect, Finlay's experiments could neither prove nor disprove the theory he had pronounced in February

1881 at the International Sanitation Conference in Washington, D. C., and half a year later before the Royal Academy in Havana.

Finlay rested his case on two premises: a) S. Ffirth's experiments disproving the contagiousness of yellow fever, and b) G. M. Sternberg's microphotographs showing unbroken erythrocytes in the extravasates without any perceptible break in the bloodvessels. The disease being not contagious and the principal lesions of yellow fever being in the vascular endothelium, the causative agent must have been confined to the vascular system and could not escape without outside help.—There were, he thought, three possible modes of transmitting the infective agent, yet on account of the work of Ffirth, only one of them appeared to be probable.[3] It had to be a very delicate instrument which in nature was routinely being inserted into man's bloodvessels for drawing blood. Thus a stinging mosquito, having by chance filled himself with a patient's blood, got its proboscis contaminated and was believed to spread yellow fever with its next meal, by piercing a blood vessel of a healthy individual. Utilizing his own epidemiological experience in Havana, Finlay inferred that of all mosquitoes the stegomyia fitted the scheme best.[4]

In spite of the wrongly accounted for time factor,[5] it was a cogent and brilliant deduction from the spare data then available. In later years, Finlay became confused on learning that the vector of Texas fever, the tick, conveyed the germ to its next generation. Finlay wrongly transferred this to the stegomyia. This is but one example of the danger of concluding *per analogiam* from experiments with different species.

Reed's experimental work started under most propitious auspices. He was in the position to utilize experiments and epidemiological observations of other research workers to a much higher degree than anybody who studied yellow fever, say, around 1880. It was already known to Reed that a) the culex, anopheles, tick, and tsetsefly were instrumental in transmitting filaria (P. Manson, 1879), Texas fever (Th. Smith, 1892/93), Nagana (Sir David Bruce, 1894) and avian as well as human malaria (R. Ross, 1897; B. Grassi, 1897/98), respectively; b) that the malaria parasite taken in with the blood entered the stomach wall of the

[3] "But the experiments of Ffirth and other considerations arising from my personal ideas regarding the pathogenesis of yellow fever, forbid my taking into account either of those modes of propagation. . . ." ((10), p. 606; (14) p. 114).

[4] In sylvan and jungle yellow fever other mosquitoes play the role of stegomyia, but this was not known for another 30 odd years (15).

[5] I. e., the mosquito's readiness for the next meal, instead of the "maturation time" of the virus in the mosquito. The question remains whether the "maturation" really requires 12 days, or is shorter, namely 9 or even 4 days, as later studies in Africa and Brazil, respectively, suggest.

mosquito and then needed 12 days before the salivary glands were reached, apparently the *conditio sine qua non* for the parasite's transmission into man's bloodvessels; c) that according to H. R. Carter (16) (U. S. Marine Hospital Service, observations 1887-1898) the time interval between a first case of yellow fever in an isolated farm house and the first "autochtonous" or secondary case in the same house amounted to 2 to 3 weeks although the incubation was known to require only 1-7 days. The time difference pointed to a "maturation period" in an intermediary host, similar to that observed by R. Ross (*sub* b); d) that the ticks too needed a "maturation period" before spreading cattle fever. Knowing all this, Reed could much better evaluate the circumstances on which the success of experimentation depended. Furthermore, the U. S. Government put very generous means at Reed's disposal.

In experiments with contaminated mosquitoes, carried out by the U. S. Army Yellow Fever Commission between December 5, 1900, and February 7, 1901, of twelve men only two remained well and ten became ill. In the second series, of five men four became sick. Finlay was consulted on the diagnosis which at that time, just as 100 years previously, depended on purely clinical symptoms. With these experiments the role of the stegomyia was established and Beauperthuy's and Finlay's theory confirmed.

It is the general consensus that the U. S. Army Yellow Fever Commission also established that vomit, stool, and soiled bedding were innocuous and epidemiologically irrelevant.

From November 30 to December 19, three persons were sleeping in the screened, mosquito-free building I (Camp Lazear) on beds covered with linen, pillows, and blankets soiled some time earlier by yellow fever patients. The room temperature was 92-94° F. Every morning bedding and garments were put into boxes and the three men left the building; every evening they returned, put pillows, blankets etc. on their beds and slept on them. They did not develop the disease. The experiments were repeated twice, on three men, then on two others, for 21 and 18 nights, respectively. There were *no* aftereffects.

Already in December, 1900, Reed wrote to his wife, "How General Sternberg [6] and hosts of others could have believed in the contagiousness of clothing and of the stools of yellow fever patients I cannot possibly see. . . . A little careful testing of this theory has served to knock it completely into smithereens." [7]

[6] "We have on record instances which appear to be authentic, of the development of an epidemic as a result of the opening of a trunk containing infected clothing. . . ." (Sternberg (5) p. 55).

[7] Quoted after Kelly (12).

As said above, Finlay relied on Ffirth's experiments. The latter name, however, does not appear in Sternberg's treatise (5), nor in the reports of the U.S.A.Y.F. Commission. It is absent also from all the Histories of Medicine [8] consulted by me, from the standard work, Strode's *Yellow Fever,* published 1951 (15), and from C. E. A. Winslow's and W. G. Smillie's chapters in the *History of American Epidemiology* (1952).

* * *

Who was Ffirth, what was his experimental record, and was he unique in experimenting on yellow fever?

On June 6, 1804, S. Ffirth presented his doctoral thesis on yellow fever to Caspar Wistar, adjunct professor of anatomy, surgery, and midwifery (17). We shall glance over the first 45 pages of the thesis rather cursorily, as only pages 46-60 have a bearing on our topic.

First the chronology of yellow fever epidemics in America (since 1535 among the Indians, and since 1612 in white settlements) was given, then the symptomatology, therapy, postmortem findings and the chemical analysis of the black vomit. Following Rush, Ffirth indulged in theoretical considerations on the difference between contagious diseases, such as measles, lues, vaccinia and small pox, and infectious diseases, like typhus, dysentery, hospital and jail fever. He discussed the role of the weather in epidemiology of a contagious disease, for instance variola, on one hand, and of yellow fever, on the other, commenting that the latter declines with the start of the cold period.[9] He further mentioned that in yellow fever epidemics the percentage of affected people was much smaller than in variola outbreaks; that in the former the physicians, nurses, grave diggers, transport workers, and washer-women very seldom fell ill, and that individuals but seldom developed yellow fever who slept with a patient prior to or following death, in the same room and even bed, without changing linen.[10] On vessels arriving from far away, say Rio de Janeiro or Santos,

[8] Such as E. H. Ackerknecht, A. Castiglioni, F. H. Garrison, C. D. Haagensen and W. E. B. Lloyd, C. C. Mettler, F. R. Packard, V. Robinson, R. H. Shryock.

[9] This was also stressed by Caldwell, Rush and others.

[10] Similar statements were made by Dr. J. Deveze of the Bush Hill Hospital (1793/4) and by others. Thus Dr. E. Miller (18) of the Bellevue Hospital in N. Y. C. asserted in his official report to Governor Lewis (January 1806): "No communication of this disease was ever observed in yellow fever hospitals, situated at a distance from the cities to which they belong. . . . The nurses at Bellevue Hospital became so entirely free from all apprehensions of the contagiousness of this disease that they often slept on the same bed with the sick, and it happened more than once, in the course of the season, that a nurse, overcome with fatigue and want of sleep, threw herself in the night, for a little repose, on the bed of a dying patient and continued there asleep until the patient was dead, and it became necessary to remove the corpse."

Brazil, with yellow fever patients on board, all of the passengers and crew who fell sick with yellow fever during the long voyage, had done so within the first 5 days after departure from the infected port of embarcation. As a rule, there were later no additional cases. Thus, Ffirth reported, the incubation period was 1-5 days and quarantine measures were unnecessary.

In 1802, Ffirth undertook experimental testing of some of the above statements, mostly using himself as a guineapig: 1) He purposely exposed himself to direct and most intimate contact with the sick. "I have several times slept all night on a bed where a patient lay extremely ill with the disease, attended with black vomit, yet never experienced any ill effects, and I made it a constant practice to receive the breath of my patients in my face, that I may ascertain its purity etc., yet with perfect impunity" (p. 50). This experiment is thus described in simple words without pomposity.

2) Ffirth fed cats and dogs one week long on black vomit; he also cut the skin of a dog, filled the subcutaneous pocket with the vomit, and closed the wound to prevent the escape of the fluid. His animals failed to get sick. This result confirmed the experiments carried out by Dr. I. Cathrall (17) in October 1799 on dogs, cats, and fowl.

3) Ffirth injected 1 oz. of black vomit into a dog's jugular vein. The animal developed convulsions and died within 10 minutes. The same happened in a control experiment with water. Convulsions and death were therefore understood to be unspecific.

4) On October 4, 1802, Ffirth started with a series of bloody experiments on himself. Upon cutting the skin of his left arm and, four days later, of his right arm, he introduced fresh black vomit, whereupon the wounds were closed. The arms were swollen and red for a few days, then the wounds healed. These experiments were repeated about twenty times (1802/3) with the very same results. No yellow fever developed.

5) A few drops of the vomit were placed in the right conjunctiva and water in the left one. No difference in reaction.

6) 3 ozs. of fresh black vomit were heated, and the vapors inhaled. No ill effect.

7) At a room temperature of 100° F., a dish with 6 ozs. of black vomit was put on a heated sand bath. Within two hours all fluid evaporated. Ffirth inhaled the vapors holding his head over the dish. Headaches, nausea, weakness, and profuse perspiration developed, but once outside

the room Ffirth rapidly recovered. Then he swallowed the thick residuary extract covering the bottom of the dish. The experiment was repeated several times, but no yellow fever developed.

Experiments *sub* (6) and (7) confirmed the negative results Cathrall had obtained on October 3, 1799. Cathrall, in his first booklet (20), 1796, believed that yellow fever was "highly contagious" and was transmitted a) by "immediate" contact, b) through the medium of air and c) by articles in which the contagion is kept and then transmitted to animated bodies. In his yard, Cathrall (19) let J. Parker (a member of the Board of Health) inhale the vapors of heated vomit and on the next day exposed himself to the vapors in a heated room. "In this atmosphere I remained one hour during which I had a constant propensity to cough and had, at times, nausea and inclination to vomit; but after walking out in the air, these effects gradually subsided. I experienced, however, a sense of weariness at my chest for many hours after." His conclusion was that "an atmosphere highly impregnated with the odor of black vomit, recently obtained, would not produce fever, apparently under the most favorable circumstances" (pp. 22-23). Thus, Cathrall, in 1799, experimentally refuted his own former (1796) belief (*sub* (b) of this paragraph).

8) Ffirth swallowed ½ oz. fresh vomit mixed with 1½ ozs. water. The experiment was several times repeated with a gradually increased amount of vomit to 2 ozs. and the dilution diminished to zero. There was no adverse reaction.

This experiment went far beyond what Cathrall had done. In October 1794,[11] Cathrall had removed black vomit from the stomach of a dead person and put a drop of it on his own lip and tongue as well as on his friend's. No yellow fever developed.

9) Ffirth made an incision in his left leg and placed four drops of blood serum of a yellow fever patient in the wound before closing it. Except for a slight inflammation there was no aftereffect of this frequently repeated experiment.

10) Saliva of a patient[12] *in ultimis*, bile, sweat, and urine were deposited in subcutaneous pockets, and the wounds immediately closed to prevent escape of the fluids. The experiments were repeated several times. No ill effects beyond temporary local inflammation.

Thus, whether Ffirth inhaled or swallowed the material, whether he deposited it in the subcutis or in the conjunctiva, whether he used fresh or

[11] I rather assume that 1794 is a printing error, the right date being 1799.
[12] Not treated with mercury.

heated black vomit, whether the room temperature was normal or elevated to 100° F., he failed to develop the disease. He, therefore, concluded: *The disease cannot be communicated by the secretions or excretions.*

Comments:

There are very few pages in the history of medicine which bespeak a heroism comparable with that of Ffirth. His experiments—bypassed by the historians of medicine and the chroniclers dealing with the conquest of yellow fever—remind us of J. Hunter's autoinoculation with syphilis and gonorrhoea and of some of J. Goldberger's deeds undertaken in order to dispose of the question whether pellagra was an infectious disease.

Ffirth's experiments were quoted by B. Rush, 1805, (21) mentioned by N. Potter, 1818, (24), but were not highly appreciated by others.

R. La Roche (6), one of the few authors who quoted Ffirth, offered on page 527 of his second volume the following comment on the contagious character of the disease, which, he said:

> . . . may be effected through other channels and agencies not yet discovered. Such experiments only show the harmlessness of these fluids, whether used in one way or another, and nothing more. They prove no more than would the ingestion of, or inoculation with, the serum of the blood, the gastric secretion, the saliva, the perspirable fluid of patients labouring under the whooping cough, scarlatina, typhus fever, oriental plague, smallpox, and other affections really or reputed contagious.

In other words, Ffirth's proof of the harmlessness of the direct contact with the secreta, excreta and effluvia was acknowledged by La Roche, but the validity of Ffirth's generalization was questioned, because there *might* exist other channels for the *direct* transmission. That, of course, is the weakness of every experimental approach not backed by a broad enough theory. However, as we know, there are no such direct channels! The idea of vectors presented by Crawford, Nott, and King[13] (USA), Beauperthuy (British Guinea), Finlay (Cuba) and by Lutz (Brazil), did not invalidate Ffirth's work, but supplemented it. Ffirth did not think of the vector channel, but experimentally disproved the existence of those—direct—channels which were supposed to exist. The gap which he left open was filled by the mosquito idea which, in the U. S. A., was pro-

[13] A. F. A. King of Washington, D. C., presented in February 10, 1882, a clear analysis of the epidemiology and prevention of malaria. Regarding both malaria and yellow fever, he connected the spread of the disease with mosquitoes plunging their probosces into patients and then into healthy persons (22). King was ridiculed. Crawford is mentioned in the article, although King was unable to get hold of Crawford's writings. King's paper is partly reproduced, without the passus on Crawford, in R. H. Major's *Classic Descriptions of Disease*, Springfield, Ill.: Charles C. Thomas, 1945, pp. 103-108.

nounced already in 1807, 1848, and 1882, but was not accepted.[14] Reed did not discover the vector channel, but provided experimental evidence for the correctness of the idea then connected with Finlay's name. Thus, Ffirth's experiments and those carried out by the U. S. Army Y. F. Commission complement one another, the one disproving the direct channels, the other proving the role of the "indirect channel," the vector.

Ffirth's and Cathrall's animal experiments were irrelevant, but experiments carried out on themselves and Parker were valid. They disproved the contagiousness—provided all three lacked yellow fever immunity. Discussing yellow fever, Cathrall clearly recognized the fact of immunity left after recovery. Had he and Parker been immune, he would hardly have carried out experiments to prove that yellow fever could not be transmitted by inhalation; these experiments would have been senseless in his own eyes.

Not as clear is Ffirth's state of immunity. In 1802, J. Henle's principle of the specific origin of infectious diseases—contagious or non-contagious —was still unknown (23). Some parasitic germs were supposed to produce only one disease, others more than one clinical entity.

Like N. Potter, J. Deveze, B. Rush, Ch. Caldwell, J. Crawford, W. D. Dewees, P. S. Physick, and others, Ffirth too believed yellow fever to be "of local origin," pointing to undrained marshes, vegetable putrefaction, stagnating water in gutters, sinks, etc. In Ffirth's words:

> . . . local causes will excite one (*scil.* disease) in a person thus exposed who is predisposed by debility, although it is not necessary that the miasma, fomes or whatever it may be that is received should produce a disease similar to that affecting a person from whom the emanation came. Thus a person receiving fomes from a dysenteric patient may have cholera, typhus, etc. Now, this can never take place in diseases that are contagious. Whoever contracted small pox from a patient labouring under measles only?

In other words, in contrast to conditions created by a contagious disease, a person who has had yellow fever might another time react to the very same causative factor with dysentery, cholera or typhus. Of course, nobody knew whether it was the very same causative agent,[15] nor whether the source was the same. All such statements were pure speculation. Like Rush in 1796, Ffirth in 1804 stated that a person could twice develop yellow fever. Had he in the past suffered from yellow fever or any ot these other diseases, is it probable that he would have concealed it?

[14] Sternberg did not even mention it in his review of yellow fever (5).
[15] In 1802 assumed to be chemical.

Would he not rather have mentioned his past history as a proof of his "predisposition" to yellow fever, as Potter did?

Ffirth's experiments, carried out with the perseverance of a fanatic, were clearly devised to answer the one and only question, whether substances secreted, excreted, or emanated, by and from yellow fever patients, carried the power of infecting persons exposed to them. Even if he did not believe in immunity as much as Cathrall, had he had yellow fever in the past, concealing the fact could have involved him in difficulties, and he would hardly have been able to defend his inaugural dissertation.

In 1901, Reed, Carroll, and Agramonte (1) wrote: "Although the literature contains many references to the failures of such contaminated articles to cause the disease, we have considered it advisable to test, by actual experiment on non-immune human beings, the theory of the conveyance of yellow fever by fomites, since we know of no other way in which this question can ever be finally determined." Were Ffirth and Cathrall included in this statement? The Commission most probably was acquainted with Ffirth's study, as Finlay, who in his first paper, 1881, (10) heavily relied on Ffirth, was in contact with Reed. Reed also was familiar with La Roche's (6) book and referred to its page 516.[16]

In any case, although between Ffirth and Reed there was a lapse of almost 100 years, there was no essential difference in the method used for disproving the role of fomites. Nor was there a discrepancy in the results of the exposure to soiled linen and soiled atmosphere between Ffirth's experiments *sub* points (1), (6) and (7), *sopra,* on the one hand, and those of the U. S. Army Yellow Fever Commission in the framed building I of Camp Lazear, on the other.

Ffirth did not transport bedding to another locality but slept several times right in the bed of the vomiting patient—without, of course, searching the room for mosquitoes. Had he acquired yellow fever, then and only then, would there have arisen for us the problem whether the transmission was direct (— contact) or indirect (— mosquitoes) and whether his conclusion was borne out by his experiments.

There is yet one item to be mentioned that might invalidate Ffirth's conclusion—without, however, discrediting his endeavors as an important scientific experimental undertaking, namely, his state of immunity discussed above. It is conceivable that at the beginning of his experiments he was immune without knowing it. On account of this possibility it would have been wiser to use other persons instead of repeating and

[16] Ffirth is mentioned and discussed prior to page 516 (*see* pp. 245 and 362) and shortly after it (*see* pp. 520, 526, and 527).

repeating experiments on himself. However, Cathrall's and Parker's inhalation experiments can well be accepted as those of other "guinea pigs." They diminish the doubts one could otherwise entertain.

Let us now return to the question whether Ffirth was unique in experimenting on yellow fever. I have already discussed Cathrall's contribution. Another precursor of Ffirth's was N. Potter (24) whose epidemiological observations were more sagacious and elucidating than his few experiments. On September 20, 1797, Potter saturated a piece of muslin with the sweat of a dying yellow fever patient "and in this condition half an hour later, bound it around my head at bedtime." No fever ensued. To prove his anticontagionistic conviction, in October 1798, Potter inoculated pus from the groin of a yellow fever patient, as well as blood, into his arms. "We have repeatedly attempted this mode of communication and have never been disappointed," is all that is said about these endeavors in his *Memoir* (pp. 52-53), published twenty years later (24). There are no details described, nor references given about any former publications. Potter himself had yellow fever in 1795, as well as in 1796. B. Rush made the diagnosis. Potter did not believe in the immunizing properties of this disease.

I am not aware of any other experimentation on yellow fever prior to 1802. In his Garrison lecture "On Anticontagionism between 1821 and 1867," E. H. Ackerknecht (25) pointed out a number of men who had carried out yellow fever experiments upon themselves. In the order given in his paper, the list consists of: Pfirth v. Salun, Lavallée, Musgrave, Potter, Chervin, Prost, Dorsey, O'Connor, Govin, Ffirth, Cathrall, J. L. Guyon, and Puhlschneider. This is not a chronological order, as the placement of Chervin and Cathrall, or of the latter and Guyon, shows. I am unable to state whether Potter, Cathrall, and Ffirth preceded all the others. In his *Short History of Medicine* (1955) Ackerknecht does not mention any one of them.

In evaluating Ffirth we must be aware of the historical setting in which he and Cathrall worked. It was almost a century prior to the start of the experimental era, of the "heroic age" of American medicine. For the U. S. Army Yellow Fever Commission it was reasonable and justified,—especially in view of Sternberg's confusion (5)—to repeat some of Ffirth's experiments on the problem of contagiousness. Nevertheless, priority and full credit regarding both the experimentation on this point and the obtained result, have to be attributed to Ffirth, or to him and Cathrall.

In one important point there is a discrepancy between Ffirth and the U. S. Army Yellow Fever Commission. Blood serum deposited by Ffirth

in his subcutis had not caused the disease, while in Cuba of twelve persons injected with blood, or defibrinated blood, or filtered blood serum, eight developed the disease. Ffirth probably used too small amounts of serum, or took blood after the third day of illness. He deposited 4 drops only, while the Commission three times injected 2 cc, six times 1.5 cc, once 1 cc, once 0.75 cc, and once 0.5 cc. Certainly, a biting mosquito does not receive, nor does it inject, between 0.5 and 2 cc, but the virus concentration in the mosquito's saliva is of another order than in the human blood, especially after the third day of sickness. After the third day even larger amounts of blood yield negative results, as experienced by Dr. Ruis in Vera Cruz in 1885/7 (5).

To stress the tremendous practical consequences of Reed's work would be carrying coals to Newcastle, but were the scientific consequences of his work of equal magnitude? Finlay's deduction from Ffirth's and Sternberg's work, and from his own observations regarding the stegomyia as the vector, was scientific truth—regardless of whether it was, or was not, believed prior to Reed's experimental proof. The same applies to Carter's (16) deduction as to the time interval in the intermediate host.

The deductive method of research proved effective not only in the field of yellow fever. Its validity and expediency regarding human malaria was demonstrated in Italy by G. B. Grassi, who without carrying out any experiment found that the anopheles, not the culex, was the vector. He proved it by logical deduction from his observations, plotting on geographical maps the proportions of all the varieties of mosquitoes in juxtaposition to the frequency, time of appearance, and prevalence of malaria (26). Just as in these two diseases, so also in other important problems it has been the deductive reasoning which brought scientific progress. Clear consideration of quantitative observational data discloses facts and associations, whereas experimental and laboratory work has frequently been but the vehicle demonstrating the truth, and sometimes even helping to distort it. An example is furnished by Ruis' experiments. Sternberg, who was present at the last of them, concluded that the yellow fever germ is *not* present in the blood but most probably in the alimentary tract. Another case in point is Galen's theory of bloodflow, based on extensive experimentation, versus Harvey's discovery based on cogent quantitative reasoning applied to old experiments and observations (Peller (27)). Sometimes experimental evidence is necessary, another time it is incidental. With respect to yellow fever in America, the experiment had the power of persuasion which the derivation of the truth by deduction lacked.

Had Sternberg in 1899, instead of setting up the second U.S.A.Y.F. Commission (1900/01), ordered Gorgas to base sanitary measures on Finlay's conception as a hypothesis, they would have been just as successful. This success, in itself, would have been experimental proof. Without Finlay's logical deduction, Sternberg would not have had any reason for doing this; that he did not do it was due to the confusion and prejudice of this technically excellent bacteriologist. Had the men in responsible positions taken pains to listen to Finlay and thoroughly examine his logic, they would have been able already in the 1880's to free the North American continent and Havana of yellow fever, without waiting for Reed's heroic endeavors. Thus, a great many people could have been saved before 1900 from sickness and death. Reed's work was necessary because Ruis' experiments obviously conflicted with Finlay's ideas and experiments, and because in our era the student of medicine is taught to be distrustful of observation and deductive thinking as long as it is not experimentally verified. Of course, sometimes deductive thinking may lead astray, but the same is true of the interpretation of experimentation and laboratory work. An example from another field is O. Folin's classic differentiation between endogenous and exogenous N-metabolism. Later, R. Schoenheimer by means of another laboratory method, namely radioactive *N*, overthrew Folin's concept (28), confirming the continuous protein anabolism and catabolism postulated by Whipple and his school.

Conclusions:

1) The experimental proof for the man-stegomyia-man cycle in urban yellow fever was for the first time rendered by the U. S. Army Yellow Fever Commission (1900/01). Moreover, the work of that Commission established for the first time that the germ of yellow fever is filtrable.

2) The first experimental proof for the non-contagiousness of yellow fever, particularly for the irrelevance of soiled linen, human secreta, excreta, and body emanations was rendered by S. Ffirth (1802/03), and partly even earlier by I. Cathrall (1799). The U. S. Army Yellow Fever Commission, using essentially the same experimental technique, thus confirmed Ffirth on a broader basis.

3) Ffirth and Cathrall fell into oblivion. That is historical injustice. Their names should be reinstated in connection with the experimental clarification of the pathogenesis of yellow fever, as they are the most important predecessors of Crawford, Nott, Beauperthuy, Lutz, Finlay, Reed and associates.

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HARVEY AND THE CIRCULATION OF THE BLOOD IN AMERICA DURING THE COLONIAL PERIOD *

F. GUERRA

During the celebration of Harvey's (1573-1657) tercentenary there was a conspicuous absence of contributions illustrating the development of his ideas in America, the way his discovery was made known in the New World, his defenders and detractors, or the effects of his doctrines upon American medical thought. Alone stand the scholarly works of Izquierdo (1936-1948) dealing with the significance of Harvey's discoveries and experimental methods in some Spanish-speaking countries, mostly Spain and Mexico. Yet many on the American Continent followed with great interest the doctrine enunciated by William Harvey in the *Exercitatio anatomica de motu cordis et sanguinis in animalibus* (Francofurti, 1628).

The evidence of the presence of Harvey's ideas in America appears in some cases only in manuscript form, but medical historians have overlooked important American imprints in the colonial period and some European works imported during the eighteenth century. These were printed in the four major languages of the cultures colonizing the New World, French, English, Spanish, and Portuguese.

French Colonies

The limited practice of medicine and the existence of only three medical imprints during the French regime in Canada account for the fact that Harvey's ideas on circulation spread into Nouvelle France mainly through the teachings of Dionis. Before his time, however, there were three monographs of great interest published in France, two by Louis Barles, *Les nouvelles découvertes sur les organes des femmes servans à la génération* (Lyon, 1674), and *Les nouvelles découvertes sur les organes des hommes servans à la génération* (Lyon, 1675), and another by Jacques Chaillou, *Recherches sur l'origine du mouvement du sang, du coeur, et de ses vaisseaux* . . . (Paris, 1664). The work of Barles not only reproduces the ideas of Harvey on the circulation, but two thirds of it is devoted

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to his ideas on generation. In Chaillou's work the circulation occupies only the first part of the book; the rest deals with milk, fevers, and humors. In both cases, however, the circulation is shown by an anatomical presentation of the heart and the four major vessels, the anastomoses, the valves of the veins, the characteristics of pulmonary alveoli, and the mechanics of the circulation according to Harvey.

It was in 1672 that Dionis was appointed by the King of France to take charge of the public demonstrations at the Royal Garden in Paris. As a result, years later he published a book of anatomy that was probably the most commonly used at the turn of the century and was the basis of the anatomical knowledge—including that of the circulation—of the French physicians. Pierre Dionis (d. 1718), a native of Paris, in his preface to the *Anatomie de l'homme suivant la circulation du sang et les nouvelles découvertes* (Paris, 1690), writes ". . . Anatomy is very much indebted to Harvey who discovered the circulation . . ."

However, only four pages of his long text are actually devoted to explaining in a very simplified form the mechanism of the circulation.

Only two other imprints may have had some influence on Canadian minds in the colonial period: the *Histoire de L'Académie Royale des Sciences* (Paris, 1666-1789) and the *Mémoires pour l'histoire des sciences et des beaux-arts* (Paris, 1701-1767) by the Jesuits of Trévoux which influenced an early Canadian publication edited by Alexander Spark, a Presbyterian clergyman, *The Quebec Magazine or Le Magasin de Québec* (Quebec, 1792-1794). In both French imprints a good description of the circulation is presented, although in the *Mémoires* of Trévoux reference to the priority of Servet is made.

We have to wait until long after the British dominion of Canada to find the first Canadian printed reference to Harvey, in the *Journal de Médecine de Québec*, 1826, where, on pages 103 and 163, there are two simple physiological paragraphs on the circulation.

English Colonies

The first record of Harvey's doctrine of the circulation of the blood in America, dated 1687 in New England, appears in a group of manuscripts originating from the teachings of Charles Morton, who earlier in his life had been at Oxford at the same time as Harvey.

Charles Morton (1626-1698), divine and teacher of renown, was born at Pendavy, Cornwall, on February 15, 1626, the son of a parson. When he was twenty years old he entered Queen's College at Cambridge, but

moved to Oxford during the Great Rebellion after Sir Thomas Fairfax, head of the Parliamentary forces, took Oxford, then the Royalist capital. Among the Oxford defenders was Harvey, physician to the King, and in those days the already famous meeting between Morton and Harvey may have occurred. On September 7, 1649, Morton was admitted a scholar at Wadham College, and in 1653, after taking his Master in Arts in the previous year, he joined the faculty of his *alma mater*.

As Morison, in the 1940 edition of Morton's work points out, Morton came during that period under the cultural influence of the Oxonian "Invisible College," generally regarded as the nucleus of the Royal Society. It is probable that from 1653 to 1675 he was engaged in some ecclesiastical enterprise; but in 1675 his life took a new course with the foundation of the Newington Green Academy, considered at that time one of the best in England. Because of academic jealousy aroused by the success of his teaching, he was accused of violating the oath taken when receiving his M. A. degree, never to teach in any university except Oxford and Cambridge, and, as an immediate result of this conflict, he sailed for New England in April, 1686, arriving at Boston the 1st of June of the same year, at the invitation of Increase Mather, then president *pro tempore* of Harvard College.

Charles Morton being *persona non grata* to the King of England, then restored, the Council of New England did not approve the appointment as President of Harvard College that Mather wanted for him, and he thus had to become pastor of the Church of Charlestown. It was there that he later arranged private philosophical lectures that attracted some students from Harvard College and brought him again in conflict with the officials of an institution. However, from 1692 to his death at 72 in 1698, he was either a Fellow or Vice-president of Harvard. As he never taught in that College, his influence was due to the high quality of his teaching elsewhere and to the spreading of his *Compendium physicae* which was used by more than a generation of students and scholars over New England.

At the time of the publication of the *Compendium physicae* (1940), 12 transcripts by his students from the original were known to survive; another four have been added in the present research, the mss. of Paine (1715), More (1709), Stoddard (1724), and Waldron (1712), all in the Massachusetts Historical Society. That Morton was acquainted with the Harvey doctrine appears repeatedly and most clearly in the text.

Hornberger, in the Introduction to the 1940 edition of Morton's text,

suggests that Morton brought a copy of his manuscript from England in 1686, that from 1687 on, it was adopted at Harvard, and that several *Theses physicae* were then based on his *Compendium*. It was probably compiled around 1680 and remained as the standard source of scientific thought in New England even after 1728, when Isaac Greenwood became Professor of Mathematics and Natural Philosophy. The work is divided into 31 chapters, following, in general, the *Organon* and the *Physicae* of Aristotle, but incorporating in some way the current problems of Descartes and Bacon, as well as several experimental achievements, such as Harvey's discoveries. Not all the copies or transcripts are suitable for the study of the circulation because in some cases, e. g. the mss. of More (1709), Waldron (1712), Brown (1714), Paine (1715), and Stoddard (1724), Harvey's doctrine does not appear in full. The following description of the circulation is quoted from Chapters 19 and 28 of the printed edition of 1940:

The 3d Concoction is Sanguification or turning the Chime into blood, and onwards into compleat nourishment of the body. The liver was antiently supposed the shop of blood, and that thither only the Chime was carryed to be perfected; but Since the Circulation was found out (by Dr. Harvey about 60 or 70 Years since) the Vogue is that blood makes blood by assimulation, for in running the rounds with it, and the blood acting all along upon [it by] its Vitall Spirit (being 10 times as much in Quantity, and 100 times [more] in Vertue) it must needs Subdue the Chyme, and conform it to its own likeness. The Circulation of the blood (whereby this act of Nutrition is performed) may be thus Explained. The Vessells of the body Containing blood, are the Arteryes and veines. The Arteries carry forth the blood hot, and vivacious from the heart to the Several parts in Every pulse; This from the Ends of the Small Capilary branches is thrust out into the flesh or Substance of Every Member, Then being percolated thro the flesh, and having left there what is fitt, and Sufficient for Nourishment it is received into the Capilary branches of the veines [passed] on by the Greater branches, and by them again is conveyed into the heart; there to receive a new Vigour. So then the Chile (or Chime) being mingled with the blood in the right Ventricle of the heart (where we last left it) it proceeds with the very next pulse (or Systole, or Contraction) of the heart through the artereous veines; into the lungs, there it is attempered with the Air of our breathing; thence it returns by the Veinous Artery into the left ventricle of the heart thence tis pressed forth into the Great Artery thence Several wayes for the Depuration, or nourishment: for Depuration into the Stomack to deposite acid humours; to the Guts, to leave there Insipid flegm, to the Kidneys for Urine; to the Liver for Gall; to diverse Grandules for Spittle, tears, [Sweat], etc: and for Nourishment to every part of the body, Externall and Internall always returning to the heart by veins which every where in due proportion do accompany the Arteryes. The Circulation in an Infant Unborn is somwhat otherwise; for the Mothers blood filling the placenta (or Secondine)

Vessel[s] it passes thence by the Navell Vein, into the Childs liver; thence by the Vena Cava (or hallow Vein) [to] the right Ventricle of the heart, thence (not to the lungs because as yet there is no [respiration] or breathing,) but by the artereous veins and a peculiar [passage] into the Aorta, and the left ventricle of the heart, thence into the great Artery, whereby it is disperced over the body sufficient for its nourishment, but the Greatest Quantity Goes forth, by the Navel Artery; and thence returns as before.

The Quantity of blood in an healthfull, and well Grown man is between 15 and 24 lb All which passes through the heart between ¼ of an hour, and 2 hours. The Quantity of blood passing in every pulse, or beat through the heart is from 1 oz. to 2 oz. the Number of pulse in an hour is from 5000 to 2000 for so much do authors differ in their Oppinions thereof. In Men that drink, [and] Urinate much some have fancied there must be a shorter way for the Liquor to pass than in this Circulation but tis said that no such wayes are found by Anatomists; and that those mentioned are sufficien [t] because the assumed liquor in such Quantity Continues not Circulating with the blood as the [62] Chile does; it is therefore not mingled with the blood, but abiding lax and disunited in the first passage by the Kidneys it falls away through its own weight.

In Women that give suck the Chile is supposed not at all to mingle with the blood, but Immediately from the Subclaviall vessels to pass (Milk as it is) into the breasts. This seams to be the best account of the 2 last concoctions, and therefore the Antients discourse (of the Chile being turned into Chime, the Chime into blood, blood into Certain humours, then Steamy dew, then Gelatine Glue which applyed to the parts to be nourished, [is] by the nutritive power converted into its Substance, all this I say) is of no Great Signification.

Puls, a particular motion of the heart, and arteries whereby in dilating and Contracting, (Cal'd Systole, or Diastole) the bloods Circulation is continued the Arteryes Still carrying out blood heated, and Impregnated with vivid Spirits, and the veines return-[89]ing it when depauperated to be again recruited (as is before noted) The Difference of Puls indicating the State of the blood and Spirits is variously distinguished by Physitians, into high, Low, hard, Soft, Even, uneven, Swift, Slow, etc.: The time of an ordinary puls is [one second], that is [1/60] part of a minute, and then there will be 3600 in an hour, but Anatomists reckon 2000 the least, [and] Some near 5000, as [Spigelius] 4876. The Quantity of blood passing the heart at every puls, is also variously accounted; Some reckon by Scruples and Drams, others by Ounces. Harvey Sayes, the left ventricle of the heart will hold 2 oz., and if all or most of this be cast out at every puls, (as the latter learned men think) and there be in men [blood] from 15, to 25 lb. then by Computation 'twill appear (taking the puls at 2000 in an hour) that all the mass of blood pass[es] through the heart [about] 13 times in an hour.

Two books, which are now of great rarity, were printed in the thirteen Colonies and contain a short account of the circulation of the blood according to Harvey's theories, although no mention is made of his name. *An Essay on Fevers, the Rattles, & Canker.* By John Walton, . . . Boston, T. Fleet, 1732. [2] 16, 8 pp., 16cms.; on pages 7-8 the writer makes a

passing reference to the circulation of the blood. The other publication is *Health. An Essay on its Nature* . . . By B. Grosvenor, D. D. The third edition. Boston, D. and J. Kneeland, 1761. [12] 223 pp., 16cms. This work was first published in London by E. Matthews, 1716. An account of the circulation of the blood, quoted from Cheselden's *Anatomy,* appears on pages 62-63.

Some years after Morton's death, the most important scientific figure of the English colonies in America became interested in the problems of the circulation and tried to explain its mechanics and reproduce its course by means of laboratory models. It was Benjamin Franklin (1706-1790), who, around the year 1745, after reading the works of Sanctorius, Hales, and others, including Harvey, maintained a correspondence with the celebrated New York physician, Cadwallader Colden (1688-1776), in respect to the circulation. Pepper (1911) has reproduced some of Franklin's letters to him; among them two (pp. 22-23), one from Philadelphia, August 15, 1745, and another of November 28 of the same year, are of considerable interest.

To Cadwallader Colden.

Philadelphia, August 15, 1745

. . . I do not remember, that any anatomist, that has fallen in my way, has assigned any other cause of the motion of the blood through its whole circle, than the contractile force of the heart, by which that fluid is driven with violence into the arteries, and so continually propelled by repetitions of the same force, till it arrives at the heart again. May we for our present purpose suppose another cause producing half the effect, and say that the ventricles of the heart, like syringes, draw when they dilate, as well as force when they contract? That this is not unlikely, may be judged from the valves nature has placed in the arteries, to prevent the drawing back of the blood in those vessels when the heart dilates, while no such obstacles prevent its sucking (to use the vulgar expression) from the veins. If this be allowed, and the insertion of the absorbents into the veins and of the perspirants into the arteries be agreed to, it will be of no importance in what direction they are inserted. For, as the branches of the arteries are continually lessening in their diameters, and the motion of the blood decreasing by means of the increased resistance, there must, as more is constantly pressed on behind, arise a kind of crowding in the extremities of those vessels, which will naturally force out what is contained in the perspirants that communicate with them. This lessens the quantity of blood, so that the heart cannot receive again by the veins all it had discharged into the arteries, which occasions it to draw strongly upon the absorbents, that communicate with them. And thus the body is continually perspiring and imbibing. Hence after long fasting the body is more liable to receive infection from bad air, and food, before it is sufficiently chylified, is drawn crude into the blood by the absorbents that open into the bowels. . . .

In another letter to Colden he continues this discussion.

Philadelphia, Nov. 28, 1745.

. . . If there is no contrivance in the frame of the auricles or ventricles of the heart, by which they dilate themselves I cannot conceive how they are dilated. It is said, by the force of the venal blood rushing into them. But if that blood has no force given to it by the contraction of the heart, how can it (diminished as it must be by the resisting friction of the vessels it has passed through) be strong enough to overcome that contraction? Your doctrine of fermentation in the capillaries helps me a little; for if the returning blood be rarefied by the fermentation, its motion must be increased; but as it seems to me that it must by its expansion resist the arterial blood behind it, as much as it accelerates the venal blood before it, I am still somewhat unsatified. I have heard or read somewhere, too, that the hearts of some animals continue to contract and dilate, or to beat, as it is commonly expressed, after they are separated from the other vessels, and taken out of the body. If this be true, their dilatation is not caused by the force of the returning blood. . . .

But Franklin went further in his research on the circulation of the blood, and tried to reproduce it with a mechanical model. There is a record of his experiment in the Diary of Manasseh Cutler, published by Cutler and Cutler (1888). In the description of a visit, of July 13, 1787, to Franklin's house in Philadelphia, we read: ". . . He showed us a glass machine for exhibiting the circulation of the blood in the arteries and veins of the human body . . ."

Spanish Colonies

There were two main foci in the Spanish American colonies where the ideas of Harvey were particularly discussed: Mexico in the viceroyalty of New Spain, and Lima in the viceroyalty of Peru. In the first, Marcos José Salgado (1671-1740), a native, wrote in 1690 a thesis, *De anathomia cordis*, and maintained in the same year a public *Disputatio de pulsibus*, but not until he printed his physiological textbook (*see* fig. 1), *Cursus medicus mexicanus iuxta sanguinis circulationem, & alia recentiorum inventa*, (Mexico, 1727), was he able to enunciate the problem of circulation in academic circles.

Salgado, who was appointed from 1722 until his death to the chair of *Prima de Medicina* at the Real y Pontificia Universidad de México, devotes leaves 179 to 217 of his treatise to explaining the problems of sanguification, motion of the heart, and circulation of the blood: " Sectio III. de chyli in sanguinem conversione," " Sectio IV. de sanguinis circulatione," and " Sectio V. de cordis motu, & pulsu." On folio 184 he says: " The discovery of the circulation . . . has been clearly demonstrated by

William Harvey. In this circular course of the blood the main factor is the heart, which drives the blood with its beat, and forces it into the arteries; and, the beat continuing vigorous, the blood, which leaves the

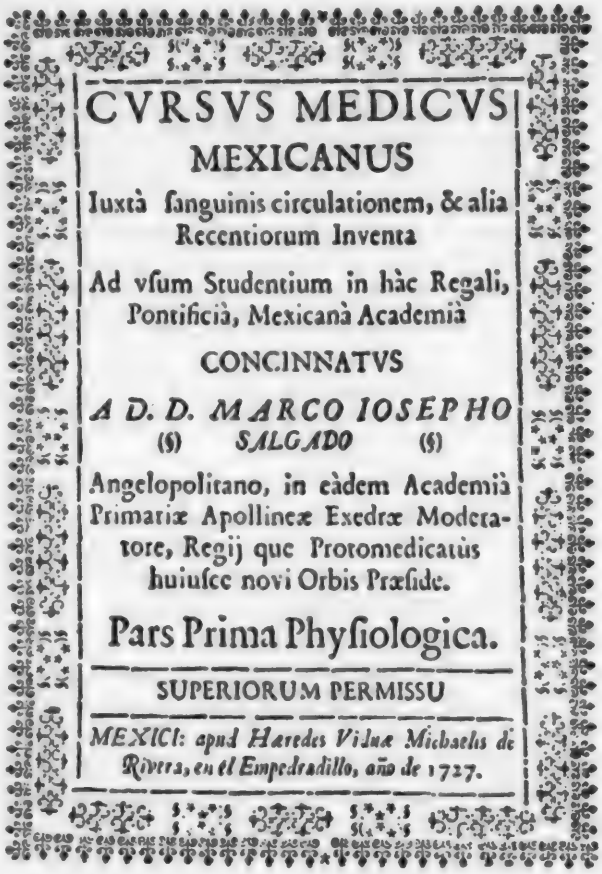
CVRSVS MEDICVS
MEXICANUS
Iuxtà ſanguinis circulationem, & alia Recentiorum Inventa
Ad vſum Studentium in hàc Regali, Pontificiâ, Mexicanâ Academiâ
CONCINNATVS
A D. D. MARCO IOSEPHO
(§) SALGADO (§)
Angelopolitano, in eàdem Academiâ Primariæ Apollineæ Exedræ Moderatore, Regij que Protomedicatûs huiuſce novi Orbis Præſide.
Pars Prima Phyſiologica.
SUPERIORUM PERMISSU
MEXICI: apud Hæredes Viduæ Michaelis de Rivera, en el Empedradillo, año de 1727.

Fig. 1.

heart through the arteries, comes back to it again through the veins . . ." He describes the pulmonary circulation very well, also the general circulation, and the movements of auricle and ventricle. He shows a tendency to reconcile the classics with the new doctrines, but denies the Galenic idea that the liver is the origin of the blood, and he is somewhat vague

about the role of the venous valves and the capillary circulation, in spite of the fact that he is aware of the writings of Malpighi.

The acceptance of Harvey's doctrine of the circulation at the University of Mexico ever since that period accounts for the fact that there were many theses *De pulsibus*, between 1721 and 1771. These have been reproduced by Guerra (1955).

The Mexican Franklin, Father Jose Antonio Alzate Ramirez (1738-1799), naturalist of many interests and publisher, like the Philadelphia printer, of several journals and works on natural philosophy, was responsible for the spreading of Harvey's doctrine at the end of the eighteenth century. In his *Gaseta de Literatura*, Mexico, 1795, he writes: " Harwei or Harveo was not the true discoverer of the circulation of the blood; Saint Ambrose in the book about Noah's ark insinuates the idea; but the English physician was the one who, thanks to repeated observations and dissections in animals, was responsible for making it clear to a point beyond discussion.

" His colleagues . . . at the beginning accused him of illusions, but, after being unable to resist his observations, came out with a clumsy song . . . that the fact was already known . . .

" It is true that Harwei was not the first discoverer of the circulation of the blood; someone supposed that it was P. Sarpi, who communicated the new idea to the physician of Aquapendente, from whom Harwei learned it; if we can believe certain sound news, the true discoverer of this mystery was the Spanish Catalonian Miguel Servet, sacrificed at the stake by the heretic Calvin.

" The physicians resisted the discovery of Harwei because they were unable to see the movement of the blood with their own eyes: the extremely useful microscope had not yet been discovered, which can show it in an infinity of insects: but, if Harwei had known that in New Spain a worm seen with the naked eye shows that rare portentous thing, would it not have confounded the incredulous . . . ?

". . . in the upper part of its body, from the head to the other extremity, there can be observed through the skin, which is diaphanous, a cylinder one line in diameter, in which can be seen the circulation of the blood, or the systole and diastole of the heart, for the blood can be seen rotating because of the undulations of the cylinder."

The worm to which Alzate refers is Maguey's worm, *Acentrocneme hesperiaris Wlk.*, which is even now used by Mexican Indians as a food delicacy.

Further south in the New World the discussion of Harvey's discoveries reaches a higher degree of erudition. According to Unanue, early in the eighteenth century Bernabé Sanchez, a physician from Lima, wrote a *Discurso contra la circulación de la sangre*, but there is no other record of this manuscript against the doctrine of Harvey; on the contrary, in 1723, Sanchez was working with Bottoni, the most celebrated defender of Harvey in South America.

The medical school at the Universidad de San Marcos in Lima, founded 1551, defended the circulation of the blood from an early date, mainly under the leadership of Dr. Pedro de Peralta Barnuevo y Rocha, who occupied the chair of mathematics. However, the most important contribution to the knowledge of Harvey on the American Continent was made through the publication of the book (*see* fig. 2) of Federico Bottoni, *Evidencia de la circulación de la sangre* (Lima, 1723). Bottoni had been born in Messina, then under Spanish dominion, at the end of the seventeenth century, and he studied medicine at Salerno. In 1702, he dedicated his *Discurso del hierro* to the Spanish viceroy in Naples, the marquis of Villena, and later went to Peru with the new Viceroy, Prince of Santo Buono, becoming interpreter of the Inquisition there and a respected practitioner. His monograph on the circulation was approved by Dr. Juan de Avendaño, professor of medicine, and Dr. Pedro Peralta, professor of mathematics, both in Lima.

In Bottoni's *Evidence of the Circulation of the Blood*, there is to be found the best presentation of current ideas in the hundred years since Harvey's discovery. He makes a complete review of the classics, agrees with Paracelsus about the chemical composition of the blood, and points out the results of Boyle, Willis, and other writers. He gives an accurate description of the microscopical constituents of the blood according to Leeuwenhoek and Hooke, the role of the insensible perspiration after the experiments of Sanctorius, the enzymatic sequences of the digestion according to Willis, the circulation of chyle after Pecquet, and finally a complete description of the movements of the heart and the circulation of the blood, making it clear that the credit for the discovery belongs to William Harvey.

There are certain points in the mechanics of the circulation where he mentions the role of previous workers, e. g. the observation of the venous valves by Fabricius of Acquapendente in 1574, and the capillary circulation and the anastomoses of Malpighi. The quality of the work of Bottoni is responsible for the fact that this Peruvian edition was reprinted in

Spain, included in the book of Francisco Suarez de Rivera, *Medicina invencible legal*, (Madrid, 1726). Among other things, few medical treatises, even in Europe, presented a similar description of the circulation of the blood, with experimental and anatomical proofs, or a better discus-

EVIDENCIA
DE LA
Circulaciòn de la Sangre.
POR
EL Doct. D. FEDERICO BOTTONI
Patrizio Meſsinés
Medico de exercizio de la Real caſsa de la Reyna Nueſtra Señora, Revisór de Libros, è Intèrprete de Lenguas, Por la ſuprèma, y Generàl Inquiſiciòn.

DEDICADA

AL
MO
R. PADRE FRAY DIEGO NARANJO, YROXAS; Lector Jubiládo, Calificadór del Santo Oficio: Examinadór ſynodál del Arçobiſpádo de Lima; Difinidór, y Padre de la Santa Provincia de Andalucía, y Comiſſario Generàl de todas las del Perú, Tierra firme, y Chile.

Con Licencia de los Superiores.
En Lima por Ignacio de Luna, en la Imprenta de la Calle de Palacio Año de 1718

Fig. 2.

sion of the knowledge and errors of the writers on the subject from Galen to Descartes, or an equally accurate presentation of the anatomy and physiology of glandular secretion. In many ways the work of Bottoni has no peer in the medical literature of that period and well deserves the transcription made by Valdizán (1928). Another careful study of Bot-

toni's work and his period was published by Lastres (1957) after the preparation of this paper.

In addition to academic support, Harvey had in Peru a popular defender of his doctrine of the circulation in the figure of Dr. Cosme Bueno (1711-1798). Born in Belber, Spain, he arrived in Peru in 1730 and became doctor in medicine at the Universidad de San Marcos in 1750. In 1758, he was appointed to the chair of mathematics, and there and in the Medical School was known as a profound student of Newton and Boerhaave. Bueno was also professor of therapeutics at the University of Lima and physician to the Inquisition. His contributions appeared periodically after 1757 with the publication, in addition to several pamphlets, of his calendars, where he always included short essays on geography, mathematics, medicine, and natural history, and chronologies. One of the calendars is of particular interest, *El conocimiento de los tiempos. Efeméride del año de 1796* (Lima, 1795), for at the end is a " disertación sobre la naturaleza del aire y sus propiedades." Of the 48 pages of this study about the properties of the air, some are devoted to explaining in an accurate way the mechanics of the circulation of the blood, its movements, the differences between the pulmonary and the general circulation, and the role of the veins, arteries, heart, and capillaries.

Portuguese Colonies

The fact that in Brazil the first medical book was not printed until 1808 explains the existence of only imported literature in Portuguese referring to Harvey. Around 1713, some exercises took place in the Medical School in Beja, Portugal, at which Joseph Lopes Pombeiro, according to the vogue of those days, tried to combine the ideas of the ancients on the circulation of the blood with the new doctrines. In the same public exercises, João Marques Correa (1671-1745) intervened to defend the views of Harvey, and his dispute was the basis of the most important Portuguese treaty on circulation: *Tratado physiologico, medico-physico, e anatomico da circulação do sangue,* (Lisboa Occidental, 1735).

In his book Marques Correa, a graduate of the Coimbra University, published a preliminary letter of Lopes Pombeiro, where the former conciliator of Galen and Harvey produces an excellent introduction to the idea of the circulation, reviewing the publications of Bartholinus, Pecquet, Willis, Boyle, Sylvius, Servetus, Harvey, and others. Marques Correa states from the beginning . . . " the circulation of the blood found in

1628 by Guilherme Harveu, English physician . . ." His book is " divided into four chapters: Chapter I. On the anatomy of the heart, veins and arteries, that go into and leave from it. Chapter II. In which are treated the marvellous movements of the heart, and their strange causes according to the ancient and the new doctrine. Chapter III. Of the true and perennial circulation of the blood in which movement, precisely, life consists. Chapter IV. In which the arguments against the circulation of the blood are dissolved totally."

The study of Marques Correa on the circulation of the blood is very well presented. He mentions the classics like Hippocrates, Galen, Fabricius ab Acquapendente, Jean Pecquet, Ettmüller, and many others, in particular the experiments of Dionis. But his most important contribution is the discussion with the Spanish physician, Mateo García, the great enemy of Harvey. In answering García's opposition to the theory of the circulation of the blood he uses the experiment of blood-letting, pointing out that García had been unable to find the valves of the veins in his dissections. The arguments of other Spanish writers, like Gaspar Bravo de Sobremonte, teacher of García, Joanini with his experiment on the circulation of the blood of the lamb, the opposite circulation of the carotid artery and the jugular vein, and, in particular, the experiments done by Harvey himself, to whom he devotes many pages, are used in the final part of his work.

Some years after the death of Marques Correa, his book, with some surgical chapters, was published in dialogue form as *Tractado physiologico-medico-phisico, chirurgico, e anathomico da circulac, am do sangue* (Porto, 1761), by the surgeon Alexandre da Cunha. The latter author, born in Villa de Mondim, Portugal, and a surgeon of Oporto, starts his dialogue:

. . . " Q. Of what else was Galen ignorant?

A. He did not have the knowledge of the circulation of the blood that in the year 1628 was found by Guilherme Harveo, English physician."

The work of da Cunha, meant for surgeons and barbers, is presented in a very clear form, mentioning the order of the discoveries and the role that every author played in the description of the capillaries, venous valves, etc.

Both works, and the general anatomical texts used in medical education in Portugal, explain why Brazilian literature of the colonial period up to 1821 accepts the doctrine of the circulation of the blood.

Discussion

It has been shown how the ideas of Harvey on the motion of the heart and the circulation of the blood appeared in America from the end of the seventeenth century; we have also seen some of the controversies provoked at the beginning of the eighteenth century, particularly in Spanish America, where the erudition and quality of the publications can hardly be matched in Europe in the same period. The New World welcomed the Harvey doctrine with its traditional liberal attitude, but every colonizing culture brought into this hemisphere some particular ingredient of its own.

In the French colonies, such as Canada, medical life and ideas were imported, and the doctrine of the circulation was just a reflection of the teachings of Dionis. His mentioning Harvey as the discoverer and his complete acceptance of his ideas, although explained in his text very briefly, had more influence in indoctrinating the medical profession of Nouvelle France than the more elaborate books of Barles and Chaillou, where great emphasis is placed on reproducing every experiment done by Harvey.

France at the end of the seventeenth century still had a large group of physicians and natural philosophers opposed to Harvey. The supporters of the circulation, as Lévy-Valensi (1933) has pointed out, were called *circulateurs,* a term which was synonymous with charlatans. In Paris, in 1652, Bertrand tried to print a book against Harvey, and the University of Paris accepted the thesis of J. Cordelle *An sanguis per omnes corporis venas et arterias jugiter circumfertur, nego* (Paris, 1670), also that of Bazin, *Estne sanguinis motus circularis impossibilis* (Paris, 1672).

The British colonies had the advantage that the controversy was already over in England, as described in the careful account by Bayon (1938 and 1939). In a new intellectual environment, like the one in New England at the end of the seventeenth century, the powerful impetus given by the *Compendium physicae* of Morton persisted all through the colonies. The students' transcripts give a good idea of the passing on of the ideas: the manuscript of Nathaniel Eells was used by the senior of that name in 1699, and by the junior in 1728, without alteration, as recorded on its blank leaf. The manuscript of William Partridge (1669-1693), made in 1688, was used by Jonathan Edwards, Sr. in 1719, and by Jonathan Edwards, Jr. in 1751.

The doctrine of the circulation according to Harvey was so powerful in American medical thought that after the middle of the eighteenth

century it was causing concern in the mind of Adam Kuhn (1741-1817), a graduate of Edinburg in 1767, who in the next year became professor of materia medica at Philadelphia; in his manuscript notes he complains that since the discovery of Harvey the action of drugs is explained exclusively through the circulation. But it was only after American independence that the Philadelphia resentment exploded in a publication. John Redman Coxe (1773-1863), pupil of Benjamin Rush (1745-1813) and successor to his chair of materia medica, published *An Inquiry into the Claims of Doctor William Harvey to the Discovery of the Circulation of the Blood* (Philadelphia, 1834), which was reprinted the same year. Coxe, opposing the admiration of Rush for Harvey, divides the credit for the discovery of the circulation of the blood among many precursors and with the ancients. In some aspects, such as the capillaries between the arteries and the veins, he does not believe Harvey enlightened the subject more than did Galen.

The situation in the Spanish colonies was completely different. Their academic institutions had a learned tradition since some universities were founded as early as 1551.

They were aware of the current discussions in Spain, and at the same time were the only Americans capable of publishing a literature of their own on the subject of the circulation. As in the British colonies, the controversy over Harvey started in the homeland, but there, it was not a problem of accepting the idea of the circulation of the blood, as most historians think; the problem was one of priorities.

This discussion has been complicated by the nationalistic attitude of Spanish writers like A. Chinchilla in his *Triunfo de la medicina española, o sea descubrimiento de la circulación de la sangre en el hombre por los médicos españoles*, (Sevilla, 1861) and, more recently, N. Mariscal in the *Participación que tuvieron los médicos españoles en el descubrimiento de la circulación de la sangre* (Madrid, 1931). On the other hand, as confessed by Bayon (1938), the opponents to the Spanish claims never read the original works. It has already been pointed out in another study by Guerra (1953), that an attitude of prejudice in an historian produces results contrary to expectations, and furthermore no sound historical research can be done without knowing exactly the context of the reference.

The controversies in Spain over the circulation of the blood were not based on the acceptance of Harvey's doctrine, which found firm support in the works of Spanish writes, like Gaspar Bravo de Sobremonte's *Resolutionum medicarum circa universam totius philosophiae doctrinam*,

tomus primus (Valladolid, 1649) and in the two monographs, that of Francisco Morelló, *Medicinale patrocinium in sanguinis circulationem* (Napoli, 1678), and of Juan Alós, *De corde hominis disquisitio physiologico-anatomica* (Barcelona, 1694). The only voice against Harvey on Spanish soil was that of the professor of anatomy at Valencia, Mateo García (d. 1691), formerly a follower of Harvey and a dedicated experimental worker who, in his *Disputationes medicinae selectae* (Lyon, 1677), after research done on the animals suggested by Harvey, like eels, frogs, and doves, was unable to find the same results, or to discover the venous valves in humans. The work of Mateo García was refuted by his Spanish contemporaries, teachers, and colleagues, and even the Spanish medical historians like Morejon (1842-1852) scorned his book. However, examining with care the huge publication of García, only a part of which deals with the *De motu cordis* and *De motu sanguinis*, it can be said that the author, instead of presenting verbal arguments against Harvey, went to the trouble of performing experiments for himself, but, like Malpighi, drew the wrong conclusions from them. As a matter of fact, the very same can be said of Harvey, as Kilgour (1954) has pointed out in a careful appraisal of the use of the quantitative method by Harvey, that no other historian had checked before. But Harvey, like Boyle, was great in the history of science in spite of the errors he committed.

Academic life in the Spanish American universities during the colonial period was more open to heterodoxical ideas than most historians realize, especially considering the state of war existing in some periods between Spain and some of the European powers. As has been presented above, it is amazing to read information on Boyle or Harvey, Cesalpino or Ettmüller, Dionis or Descartes, or comments on the current proceedings of the Royal Academy, in the works of those days, printed in Mexico or Lima.

The Portuguese authors also had some opponents in presenting the findings of Harvey. Bitter criticisms of Cunha's book appear in the *Gazetta litteraria de Lisboa* (1761, *1*, 343-348) by the editor, Francisco Bernardo de Lima, and the physician, Manoel Gomes de Lima. But perhaps Cunha's book had a strange power over its readers, for among the licences of the Holy Inquisition was one from Fr. Antonio dos Remedios whose censorship results in a long and careful presentation of the ideas on the circulation, and on the predecessors and followers of Harvey.

In the original study of Marques Correa, the licenses of the Holy

Inquisition are all favorable, but lack such a presentation and include only the introductory letter of Lopes Pombeiro. The license accorded by Cypriano de Pinna Pestana, physician to the King Joam V of Portugal, expresses a knowledge of the doctrine of Harvey and other contributors to the discovery of the circulation of the blood.

This incidental mention of the role of Fr. Antonio dos Remedios, *definidor* of the Holy Inquisition in Portugal, in promoting the spreading of Harvey's ideas in the Portuguese dominions, brings to mind the point that all the defenders of Harvey in Spanish America were, like Bottoni, members of the Holy Inquisition. Nevertheless, some historians without proper study of these facts blamed the *Santo Oficio* for impeding a better understanding of Harvey's doctrine in the Spanish colonies.

Summary

Harvey's doctrine on the circulation of the blood was known during the colonial period through this literature imported from France into Nouvelle France, and from Portugal into Brazil. New England was the first American territory to know the discoveries of Harvey in full detail from the earliest teachings of Morton in 1687, preserved in manuscripts for future generations. However, no printed literature appeared on the subject. The Spanish American colonies, particularly the cities of Mexico and Lima, had an important literature of their own from the beginning of the eighteenth century, a literature that compared favorably with publications appearing in Europe. In this respect the physicians and members of the Holy Inquisition contributed to the spreading and defence of Harvey's ideas.

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PIETRO PISANI AND THE MENTAL HOSPITAL OF PALERMO IN THE EARLY 19TH CENTURY *

GEORGE MORA

Sicily, the crossroads of many civilizations which occurred successively in the Mediterranean, has maintained throughout the centuries a strange, passionate character, which defies any formula or any generalization. This island, " the most beautiful, wild and romantic country in the world," to repeat the expression of P. Brydone, the famous author of *A Tour through Sicily and Malta,*[1] (1773), has retained a mysterious appeal, impossible to define, and has exercised a particular fascination on the many travellers who, beginning with Goethe,[2] discovered it in the late 18th and the early 19th centuries. Perhaps one reason for the difficulty in understanding Sicily is that this island has paradoxically remained almost untouched by three of the major forces operating in European history: the Roman universal influence, the Italian Renaissance, and the French Revolution.

Events of importance for medical history have, of course, been studied and placed in the right perspective by specialists. Perhaps the most significant one is the flourishing of the medical schools of Messina and of Palermo, where G. B. Cortesi, G. A. Borelli, P. Castelli, M. Malpighi and G. F. Ingrassia taught, in the middle of the 16th century. A century later, during the period of cultural depression coincident with the Spanish domination, this brillant tradition had already been extinguished.[3]

It is no wonder that the next major event, the development of the mental hospital of Palermo under Pietro Pisani, has been almost completely overlooked by medical historians as well as by psychiatrists. The early history of this hospital, as is the case with many others, is surrounded by obscurity and uncertainty. It is known, however, that during

* Presented at the thirty-first annual meeting of the American Association for the History of Medicine, New York, N. Y., May 23, 1958.

[1] P. Brydone. *A Tour through Sicily and Malta.* London, 1773.

[2] Goethe left a description of his visit to Sicily in 1787 in his *Italienische Reise* (1816-1817), frequently republished and translated.

[3] On the history of medicine in Sicily, see: G. Pitré. *Medici, chirurghi, barbieri e speziali antichi in Sicilia, sec. XIII-XVIII.* Roma, Casa Editr. Libro Ital., 1942; *Idem, La vita di Palermo cento e più anni fa.* Palermo, Reber, 1911; S. De Renzi. *Storia della medicina in Italia.* 5 vols., Napoli, Filiatra-Sebezio, 1845-1849.

Portrait of Pisani from *Il Pisani*, 1878, p. 1.

the middle ages mentally sick patients were placed in a hospital for lepers (San Giovanni dei Lebbrosi) erected by William I, the Norman, in the 12th century. In 1219, Frederick II placed this hospital under the care of the Teutonic Order, and two centuries later, in 1419, it was placed under the care of the Senate of Palermo. In spite of the efforts made by Queen Maria Carolina of Austria to move the mental patients to a more suitable place, their condition remained very unsatisfactory at the beginning of the 19th century.[4] It was finally in 1824 that Barone Pisani, being officially asked by the government, agreed to dedicate all his energy to the reform of the treatment of mental patients.

Barone Pisani,[5] born in 1760—thus 64 at that time—was already well known in Palermo for his philanthropic work. The son of a tax collector of the Kingdom of Sicily, Barone Pisani was short and heavily built; his aspect was severe, and his eyes were penetrating and eloquent. He first studied jurisprudence, but, artistically minded, he turned to music and archeology.[6] After his marriage in 1784, his home became a favoured meeting place for musicians and artists, including the famous poet Giovanni Meli, the so-called "Sicilian Anacreon," who was also a well known physician in Palermo.[7] Following the death of his son Antonio, a precocious musician, in 1815, Barone Pisani entered a long period of depression and finally decided to dedicate himself entirely to humanitarian work. It was this decision that brought him to work in the island's ministry of the interior and finally to accept the superintendency of the hospital for mental patients, in 1824.

It would be important for medical historians to trace the possible forces which were operating at that time in Sicily in the direction of the reform of the treatment of mental patients.[8] Local enlightening forces,—

[4] See: *Nuovi capitoli ed istruzioni dello Spedale di S. Giovanni de' Leprosi, filiale del Grande Spedale di questa città di Palermo.* Palermo, 1741.

[5] On the life and work of Barone Pietro Pisani: A. Linares. *Biografie e ritratti d'illustri siciliani morti nel cholera l'anno 1837.* Palermo, Alleva, 1838; B. Serio. *Biografia del Barone Pisani.* Palermo, Roberti, 1839; *B. Salemi-Pace. Cenni biografici sul Barone Pietro Pisani.* Palermo, Virzì, 1878; "Pietro Pisani," in *Dizionario dei Siciliani illustri.* Palermo, 1939. See also: E. W. Güntz. *Don Pietro Baron Pisani, der Vorläufer John Conollys.* Leipzig, Reklam, 1878. For Pisani's bibliography: G. Mira. *Bibliografia siciliana ovvero gran dizionario bibliografico delle opere edite ed inedite, antiche e moderne di autori siciliani.* 2 vols., Palermo, Gandiano, 1875-1881.

[6] See: Pisani. *Memoria sulle opere di scultura in Selinunte,* ultimamente scoperte da Pietro Pisani, ufficiale di ripartimento nella Real Segreteria presso il Luogotenente Generale di Sicilia. Palermo, 1824.

[7] On the physician Giovanni Meli: G. Pitré. "Giovanni Meli medico e chimico." *Archivio storico siciliano,* 1907, n. s. *32*: 1-43.

[8] On the political, economic, and cultural conditions of Sicily at that time, see especially:

such as the program of medical treatment of the poor, initiated by the "Accademia degli Jatrofisici" in 1770 and partially carried on in the "Albergo dei Poveri," which was mentioned by the great Sicilian historian G. Pitrè in his monumental work,—were present, but not in the field of mental diseases. The news of the reform of the treatment of these diseases, already initiated in Florence by V. Chiarugi, in Paris by P. Pinel, in England by W. Tuke, could have perhaps been brought to the island by the numerous artists, scientists, and scholars who visited it at that time. Pisani himself, as reported by his biographers, had travelled throughout Europe in his youth, although it is not known where and when. Therefore, any attempt to place the reform of the mental hospital of Palermo in the right historical perspective has to be postponed until further material becomes available to the historian. For the moment, the external influences which could have contributed to Pisani's humanitarian work remain unknown. It is not improbable that the inner emotional experience caused by the death of the beloved son, and the subsequent period of depression, constituted the final stage of a process long maturing in Pisani's sensitive and intuitive personality.

As an indication of this personality, it is sufficient to quote Pisani's original description of his first visit to the old hospital of Palermo, in his own lively and dramatic terms:[9]

> The condition of abandon in which I found this place was absolutely unbelievable. It gave the impression of being more of a menagerie for deer than a home for human beings. The patients were locked all together, no matter what their condition was, in a few dark and unhealthy cells. They were lying on straw or directly on the floor and they were almost completely naked. They were suffering from hunger and from cold and they were submitted to physical punishments. Furthermore, many of them were affected by physical diseases, being in close contact with tuberculous, leprous and dermatological patients.
>
> Deeply touched by such a horrible spectacle, and stimulated by an intense desire to help those poor people, I tried to approach them, but I was repelled by the unbearable smell. My first act was to break and throw away those terrible chains which tied those people almost completely. Then I started to encourage them and to offer them food and wine. As soon as they started to feel a little better, they got up and threw their arms around those who had liberated them. . . . Their pale and skinny faces were animated by new life and even their eyes, full of joy, expressed gratitude. . . . It seems as of that moment insanity had been replaced

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A. Genoino. *La Sicilia al tempo di Francesco I (1777-1830)*. Napoli, Guida, 1934; V. Titone. *La cultura siciliana nella seconda metà del sec. XVIII*. Palermo, 1946; and G Pitré. *Opere complete*. Casa Editr. Libro Ital., Roma, 1940 and foll.

[9] The following quotations are taken from passages of the above-mentioned biographies of Pisani. Italics mine.

by reason and gratitude. . . . The patients were later provided with clothes and beds. I finally made sure that not only physical punishments, but even derogatory words and criticism were strictly forbidden. In this way a success had crowned the first step of the *moral treatment* which I had had in mind to gradually establish in the hospital and which is *the only hopeful treatment of mental patients.*

It soon became evident that the present facilities of the hospital were not appropriate for such a program of treatment. It was necessary to enlarge the hospital, to build new units, and to organize the various services of the hospital. Pisani's concern was to achieve a solid structure offering security for the patients, but in a way that the appearance would be very different from that of a prison. Therefore his suggestion was "to make the building nice looking through decorations and embellishments, so as to raise joy in those patients affected by continuous depressions." This was Pisani's plan of improvement of the institution, "to make it suitable for moral treatment."

Pisani accomplished his ambitious program in less than three years, in spite of great financial difficulties which were largely due to the lack of understanding on the part of the Bourbon dynasty. A new building was erected 1½ miles from Palermo. It was divided into two floors, the upper for the private patients, the lower for the others, under the charge of cities and towns. Male patients were separated from female. The facilities of the building included running water and baths. The full capacity was 200, although probably the average number of patients, according to the reports of many, was 140. Every detail was considered to make the atmosphere of the place as pleasant as possible: for instance, the walls were covered by beautiful and cheerful paintings.

Even more important than this, are the *Istruzioni* (*Regulations*),[10] written by Pisani in 1826 and published the following year, which give an idea of his intuition and his good judgment, remarkable in a man who was not a physician. It is sufficient to report here some of Pisani's points. In spite of the fact that the care and cure of the patients was based on moral treatment, all medical technical devices were applied by the staff in the best possible way. "It is important to make the patients understand that their fate is completely in the hands of physicians, in order to remove from their mind the sad idea that insanity is a condition absolutely untreatable, as many people erroneously believe." The director was personally responsible for the moral treatment of the patients. A restricted number of physicians were full-time at the hospital and rounds were made

[10] P. Pisani. *Istruzioni per la novella Real Casa de' Matti in Palermo.* Palermo, 1827. A German translation of this work appeared in: Güntz, *op. cit.*, pp. 22-40.

by them every other day. Male and female nurses and attendants were on duty at all times, and their relationship with the patients was considered particularly important. Progress and treatment notes were written at regular intervals. A conference of the superintendent and the physicians concerning the treatment of each patient was held weekly and at the end of the hospitalization period. An autopsy was performed on each patient who died in the hospital, and the brains were preserved in the pathological museum. All the observations and remarks gathered from the study of the patients and of the pathological material were published in a special journal.

An absolute condition was that the hospitalization of each patient had to be approved by the Lieutenant General of Sicily. The persons accompanying the patient were to bring a note containing the essential biographical data of the patient. Information regarding the family of the patient and the possible cause of the mental condition was to be available, and considered, of course, as strictly confidential. As soon as admitted, the patient was given a bath and then shown around the hospital by the physician, the nurse, and the attendant. In the early days after admission, particular attention was given to the patient, and more detailed observations were gathered. A special effort was made to render the patient as comfortable as possible through continuous reassurance and a constant impression of serenity. *"In fact, in spite of their mental disorder, patients respond to a frank and sincere approach and are able to experience feelings of confidence, benevolence, friendship, and pride."* [11]

In another passage of his *Regulations* Pisani stated that "the basis of the moral treatment is the separation of the patients from their families," as "observation has indicated that patients never improve in their family environment, because that is where the cause of their troubles is located." In line with this, relatives were not allowed to visit patients in the hospital, until they showed a substantial improvement. The expressions and the tendencies of the patients were studied in order to come to an understanding of their condition. Through affectionate and lovable manners their minds were removed from their fixed ideas, and, instead, interested in the good and moral principles which lead men to society. The moral approach, of course, was not limited to the superintendent of the hospital because—to quote Pisani—"all the employees, from the first to the last one, have an essential part in the treatment and the cure of the patients."

Of the different methods used to break the vicious circle of the distorted

[11] Italics mine.

ideas of the patients and to sustain their attention, constant work was in Pisani's idea the most efficient. "Regular work reinforces the attention of the patients, regulates their blood circulation, and makes them relax and sleep better." For this purpose manual tasks were encouraged in the institution, especially those having relation to the work previously done by the patients. The first preference was given to farm work, because "the natural inclination of man toward earth helps, as mental patients, no matter of which class, willingly take part in farm work, especially when adequately supervised." Women took part in work in the garden, this being appropriate work for them. Another useful measure was to employ male and female patients in the internal service of the hospital, according to their capacity. The little money given to patients helped them to meet their needs. However, for no reason were patients asked to do things as servants, not even small tasks.

Furthermore, an extensive program of dances, physical exercises, songs, and dramatic presentations was organized for male and female patients in the institution. The patients were continuously encouraged to get along with each other and to consider themselves only as unlucky individuals, not different from others. Responsibility was given to patients according to the degree of improvement. Patients were allowed, for instance, to receive visitors and to take them around the hospital, to go into town by themselves or with others, to the theatre or to shop. When improved enough, patients were allowed to return home for a trial period of three months, and then indefinitely. All systems of restrictions were abolished, except temporary isolation of the violent patient in his own room, and the straight jacket, which was later abolished and replaced by a tepid bath. In extreme cases of agitation, the method found by Pisani to be the most efficacious was to tie the patient securely to a hammock in a specially padded room and then rock him like a child until he fell asleep (see letter by Pisani to Dr. Moore of London).[13]

In considering now Pisani's work in its totality, and considering that Sicily was at that time—and still is to a certain degree—in very poor economic condition, that its society was still of a feudal type, and that social institutions were still very primitive, one should not be surprised to learn that a legend was created around Pisani's personality. Both this legend and the scarcity of historical material of scientific validity are responsible for the difficulties in establishing the real historical dimension of Pisani's reform. Many visitors to the island were attracted by Pisani's reputation, but more as a matter of curiosity than of scientific investiga-

[13] This letter, written on Dec. 11, 1835, is reported by Serio, *op. cit.*, pp. 82-83.

tion. In spite of the fact that Pisani continuously tried to protect his patients from the curiosity of the indiscreet, a special guide to the institution—interestingly enough, ideated and written by a former mental patient—had to be specially printed,[13] and illustrious visitors such as Lord Buckingham, were shown around by recovered patients.[14]

The reaction of the visitors to Pisani's institution was, of course, different, according to their personality, cultural background, and special interests. Perhaps the extreme was reached by Edward Baynes, an English writer, who described Pisani, as "an old nobleman, a very witty, kind philanthropist, who had only one strange idea, that of curing the insane."[15] Many other visitors, even laymen, were very much impressed by the humanitarian reform introduced by Pisani, as reported by H. Tuzet in her two extensive studies on foreign visitors to Sicily in the 18th and 19th centuries.[16] Palmieri di Micciché expressed his astonishment that "such a fine institution, so well conceived and directed, where so many marvellous cures were taking place, in a word such a model institution," could be located in a very poor and primitive country.[17] William R. Wilson, an English visitor certainly quite critical of contemporary Italian mores, left a detailed and sympathetic description of Pisani's institution, emphasizing "the excellence of the institution itself and the admirable system of management and care observed in it, which both reflect the highest credit on the skill and humanity of Baron Pisani." He concluded by stating that "it is impossible not to be struck with the admirable discipline, order and regularity that prevail in every part of this truly excellent establishment."[18] Marmont, maréchal de France and duc de Raguse, stressed especially the humanitarian spirit underlying the therapeutic systems and the good results accomplished in the mental hospital of Palermo, "an institution unique in all Europe." He suggested that the different governments of Europe should use this institution as a training place in order to improve the condition of their mental hospitals.[19]

[13] *Guida pe' forestieri che si fanno a visitare la Real Casa de' Matti in Palermo, scritta da un frenetico nella sua convalescenza.* Palermo, Muratori, 1835.

[14] Serio, *op. cit.*, p. 82.

[15] E. Baynes. "Sycilian facts. "*Metropolitan Magazine* (*London*), 1834 (?), French translation: "Esquisses siciliennes." *Revue britannique.* 3ème série, 1834, pp. 300-323.

[16] H. Tuzet. *La Sicile au XVIII siècle vue par les voyageurs étrangers.* Strasbourg, Heitz, 1955; *Idem, Voyageurs français en Sicile au temps du romantisme* (*1802-1848*). Paris, Boivin, 1945.

[17] M. Palmieri di Micciché. *Pensées et souvenirs.* Paris, chez l'auteur, 1830, pp. 228-234.

[18] W. R. Wilson. *Records of a Route through France and Italy.* London, Longman, 1835, pp. 270-273.

[19] A. F. L. V. de Marmont, maréchal de France and duc de Raguse. *Voyage en Sicile.* Paris, Ladvocat, 1838, pp. 210-212.

Alexandre Dumas, the elder, was also interested in the treatment of mental patients and left a description of the dramatic presentations held in Naples by mental patients, as reported in a previous paper.[20] Although his biographers accuse him of frequent inaccuracies and of mixing reality with fantasy, it appears, from the chapter "La maison des fous" (included in his book *Le capitaine Aréna*), that he visited Pisani's institution in 1835.[21] As is the custom with Dumas, his description is characterized by grandiosity and imagination. However, it does not present any new element, except perhaps in the colorful scene illustrating the sedative effect of music on two agitated patients. More valuable and complete, even though concise, is the anonymous report on the mental hospital of Palermo which appeared in the Swiss newspaper *Le Fédéral* on May 25, 1832, where the institution is described as "one of the most remarkable of this kind" and Pisani as "one of the greatest benefactors of mankind."

No matter how interesting are the reports of these authors, however, more valid for medical historians are the descriptions left by physicians, and especially by psychiatrists, who visited Pisani's institution in good number in the second decade of the past century. Pisani's biographer, Bernardo Serio, gave a detailed list of these physicians as well as of other learned people, which obviously cannot be reported here. Mention can be made here only of Martin W. Mandt and Carl Rust, two distinguished physicians important enough to be mentioned in the *Allgemeine Deutsche Biographie* by E. Gurlt, who were officially sent to Italy by their Prussian government for a scientific tour in 1832.

The report of their tour[22] is remarkable for its emphasis on the

[20] G. Mora. "Dramatic presentations by mental patients in the middle of the 19th century and A Dumas' description." *Bull. Hist. Med.*, 1957, *31*: 260-277.

[21] A. Dumas, père. *Impressions de voyage. Le capitaine Aréna.* Paris, Calmann-Lévy, 1881, pp. 1-24. See also: *La vie d'Alexandre Dumas*, racontée par A. Dumas. Textes recueillis par A. Guerin. Paris, Juillard, 1953, pp. 213-221.

[22] Mandt and Rust left a report of their visit to mental hospitals of Italy, France and England in the Preussisches Geheimes Staatsarchiv (Krankenhäuser und Anstalten, Generalia Nummer 18, 1833). This report was recently published in condensed form by H. Hoffmann, "Ein Beitrag zur Geschichte der Psychiatrie," *Allgemeine Zeitschrift für Psychiatrie*, 1935,*103*, 76-127. (The author is grateful to Prof. Dr. W. Artelt of the Institute of History of Medicine of Frankfurt am Main, Germany, for drawing his attention to this important paper). On Mandt: G. Bandiera. *Notizie biografiche del cavaliere Martino di Mandt, medico della imperatrice delle Russie.* Palermo, 1846; Veronika Lühe. *Ein deutscher Arzt am Hofe Kaiser Nikolaus I. von Russland. Lebenserinnerungen.* München-Leipzig, 1917; F. C. Erichsen. *Martin Wilhelm Mandt (1799 1858). Abhandlungen zur Geschichte der Medizin und der Naturwissenschaften*, 1936, Heft 10. On Rust: Calissen, *Medizinisches Schriftstellerlexicon der jetzt lebenden*

humanitarian—namely "moral"—treatment of mental patients and on the practical ways of introducing it in mental hospitals. Many important points—separation of mental from mentally retarded patients, subdivision of patients in the hospital according to their needs, principles of construction of mental hospitals and their location, training of personnel for such institutions, up to the debated question of the moral versus the physical causes of mental conditions—are thoroughly analyzed and discussed, frequently anticipating views which were later to be accepted by most psychiatrists. Of all the hospitals visited, including the private institution of Esquirol at Ivry and the Maison de Charenton in Paris, Mandt and Rust were especially impressed by the one at Palermo, which they considered to be of particularly high standard.[23] They described in detail "the splendid results of a systematic, individualized and flexible occupational program for mental patients in the beautiful institution of Palermo, the memory of which was still so vivid in their minds," [24] and they felt that perhaps such a program was a late result of old Arabian views.[25] After a full German translation of Pisani's "Regulations," they. like all other visitors, expressed admiration for Pisani's tremendous personality.[26]

He sacrified each personal interest to the welfare of the institution. Endowed with a high degree of sensibility, an exceptionally good disposition, a very clear and unprejudiced understanding of the importance and of the difficulty of the project, he dedicated his entire energy to the institution. He lives there among his patients, studies their individuality, their pathological conditions and their habits and—with his stable, friendly and composed attitude—always obtains respect and consideration even from patients in states of agitation.

Finally, Mandt and Rust reported four basic aspects of Pisani's moral treatment: 1) the essence [namely the dynamic] of the mental patient is not expressed by the manifestations of the disease; 2) psychic functions should be stimulated as little as possible; 3) each mental patient must be brought to believe that he will be treated like any normal individual; 4) the most important method of treatment in this beautiful institution is

Ärzte, Wundärzte und Geburtshelfer, Kopenhagen, 1833, Bd. 16, p. 438; Altona, 1844, Bd 32, p. 52. See also: F. W. Bayer. *Reisen deutscher Aerzte ins Ausland (1750-1850). Abhandlungen zur Geschichte der Medizin und der Naturwissenschaften*, 1937, Heft 20; W. Artelt, *Einführung in die Medizinhistorik*. Stuttgart, Enke, 1949, p. 85.

[23] Hoffmann, *op. cit.*, p. 124.

[24] Hoffmann, *op. cit.*, p. 88.

[25] Hoffmann, *op. cit.*, p. 120.

[26] Hoffmann, *op. cit.*, p. 107.

to keep the patients continuously occupied.[27] They only regretted that Pisani was not a physician himself, and therefore not able to diffuse his principles more adequately.

The authors so far mentioned all visited Palermo's institution during the decade of Pisani's superintendency, between 1826 and 1837. Pisani, during this time, continued his humanitarian work without interruption and furthermore attempted to base it on solid scientific ground. According to his biographers, he studied all the books he could find in the field of psychiatry, such as the works of Willis, S. Tuke, Pinel, Esquirol, Spurzheim, Gall, and Georget, and books on the institutions of York, Bedlam, Bicêtre, Salpétrière, Charenton, and Aversa. He performed autopsies and found no difference between normal and insane. He divided the causes of mental conditions into congenital and acquired, and the latter into physical and emotional. As emotional causes he considered—to quote William R. Wilson—" terror, love, jealousy, deep sorrow from loss of children or parents and reverses of fortune." [28]

Endowed with fine clinical intuition—as B. Serio wrote—" he did not base his actions on abstract theories, but on facts, and did not apply the same principles to everyone regardless, but according to the different personalities of the patients." His idea—which unfortunately could not be accomplished—was to write " a great work about the practice of moral treatment ,emphasizing not so much its general principles, but rather the remarkable results obtained through it in individual cases during several years of experience." In a letter to a friend,[29] he wrote that he wanted to describe in detail in such a work the different methods employed in the treatment of mental patients. In the same letter, however, he stated that his institution was far from being completed and far from the degree of perfection that he had imagined, but that progress was made, even if slowly. . . .

In the meantime, the institution continued to be visited by many, like Lord Buckingham who considered Pisani superior to Howard,[30] like the French psychiatrist Etienne Pariset, chief of service at the Salpétrière, who considered Pisani the best qualified authority on moral treatment,

[27] Hoffmann, *op. cit.*, p. 108.
[28] Wilson, *op. cit.*, p. 271.
[29] Serio, *op. cit.*, p. 84.
[30] John Howard (1726-1790), the famous philanthropist and reformer of the English prison system, visited extensively the main correctional institutions of many European countries and left his observations in his two books, *The State of the Prisons in England and Wales*, Warrington, 1777, and *Account of the Principal Lazarettos in Europe*, Warrington, 1789.

and like the German psychiatrist Edward W. Güntz who—taken ill in Palermo—was received by Pisani like a son and in turn considered him a second father for the rest of his life. Other psychiatrists, like Esquirol, though very anxious to visit Pisani's institution, never had the chance to do so.[21]

All these visitors were impressed by the strong influence that Pisani had personally achieved on his patients. Many of them reported that the very presence of Pisani was sufficient to quiet down even very agitated patients and that the greatest preoccupation for any patient was the fear of losing Pisani's favour. It is reported by several authors that, on the occasion of an illness which kept Pisani at home for some days, a state of agitation developed among the patients of the hospital. Finally, things improved again when a delegation of patients was admitted to Pisani's home and allowed to see him personally.

The question naturally arises, how many and what kind of patients improved while treated at Pisani's institution. As with other hospitals of the time, statistical details of the work carried on in his institution are not adequate. However, it is worth-while to report the data collected by Antonio Greco, physician of the hospital, as published by Marmont, maréchal de France and duc de Raguse.[22] While at the beginning, in 1825, the institution received 67 patients, in 10 years the total number was 504. Of these, women were twice as numerous as men, and quite a few were children under 15 years of age. Of a total of 468 patients, 293 were diagnosed as manic, 89 as monomanic, 70 as dements and 6 as idiots. Melancholic patients belonged mostly to the upper class, while the manic and dement belonged mostly to the middle and lower class. Of a total of 401 patients treated in 10 years, 160 (namely 2/5) were discharged as cured. According to Pisani's biographer, B. Serio, this proportion of cures was superior to that of 1/5 obtained at Charenton and of 1/3 at Bicêtre and Salpétrière in Paris. It was Pisani's experience that if patients did not improve during the first eight months of hospitalization, they were to be considered prognostically as poor cases. Finally, of the different diognastic categories, mania and monomania had a better prognosis and a lower mortality than melancholia and dementia.

No matter how difficult it is to translate these data into modern terms, the fact remains that the rates of cure and improvement at the Palermo institution were considered as exceptionally high by all visitors, including

[21] Güntz wrote in fact to Pisani that Esquirol was very anxious to meet him and to visit his institution (See Salemi-Pace, *op. cit.*, p. 57).

[22] Marmont, *op. cit.*, pp. 297-331.

psychiatrists. This explains the enthusiasm of many of them, as attested by several facts. William R. Wilson introduced Pisani's ideas into Scotland.[33] Dr. Moore, personal physician of Lord Buckingham, proposed to translate Pisani's writings into English.[34] Pisani's institution was taken as an example by the mental hospital of Geneva in Switzerland [35] and that of Worcester in this country.[36] In two letters of 1834 and 1836, a Dr. Francis G. Shaw of Boston reported the admiration of the newly opened Worcester Lunatic Hospital and of the Boston Phrenological Society for Pisani's work.[37] Pisani, who in the meantime had been nominated a member of several academies, including that of Leipzig and the Royal Academy of London, was made an honorary member of the Boston Phrenological Society on April 2, 1836. The original document reads as follows:

Sir—It has long been the wish of the Boston Phrenological Society to testify to you its high sense of the value of your labour in the cause of science and humanity. It has been the unanimous wish of the members that the honorary degree of membership should be forwarded to you; and it would have been done, if it were certain that such public notice would have been advisable or agreeable to your feelings. The Society however was anxious to rank you among its honorary members, not with a view of conferring honour upon a name so widely honoured, and so highly valued, but of giving you a testimonial of its respect: for this purpose perhaps you will esteem a simple letter as efficacious as a formal diploma; and you may regard this as such.—I forward to you some of the publications of the Society, of which it begs your acceptance.—Allow me to make use of this opportunity of assuring you of our respectful esteem.—Samuel G. Howe, Secretary, Boston Phrenological Society, Boston, April 2, 1836.[38]

Pisani had reached the highest level of his renown at that time. But he was already old, well over seventy, and the end of his life was approaching. Actually, many lives—more than twenty thousand—were taken in Palermo in that year of 1837, when cholera violently struck the city for the first time in its history. Pisani's wife was one of the first to succumb to the deadly disease. Barone Pisani, instead of being overcome by grief, found new energy to give to his patients, now that he no longer had a home. In the last few weeks of his life, he remained day and night in the hospital among his beloved patients, who—because of the exceptional

[33] Serio, *op. cit.*, p. 51.
[34] Serio, *op. cit.*, p. 52.
[35] Serio, *op. cit.*, p. 93. See also: "Hospice d'aliénés à Palermo." *Le Fédéral, Journal genevois*, May 25, 1832.
[36] Serio, *op. cit.*, p. 93.
[37] These letters are reported in the original Italian by Serio, *op. cit.*, pp. 95-96.
[38] The document is reported in the original English by Serio, *op. cit.*, pp. 96-97.

conditions—had been almost completely abandoned by the staff. In spite of the precautions taken, the infection invaded the hospital, too, and Pisani died of it on July 6, followed soon after by thirty-two of his patients.[39]

His fame, however, did not end with his death. In the same year of 1837, the historian Antonio Linares gave a short biography of him in his report on the well-known Sicilians who perished during the epidemic of cholera.[40] Two years later, in 1839, Bernardo Serio wrote an extensive monograph on Pisani, which still remains basic for the comprehension of his work and of the impact that it had on his contemporaries.[41] In general, however, the response of Italian psychiatry to Pisani's work was extremely meager. Probably, one main reason for this was that his work could not be appreciated in a period when psychiatry was affirming its dependence on neurology. Pathology was to dominate the entire field of medicine for the next decade and, similarly, psychiatry was to be concerned only with cerebral functions. It is evident that from such a viewpoint, Pisani's moral treatment had no scientific validity and, at the most, could be considered as a commendable effort made by an amateur in the field of psychiatry. This viewpoint, of course, did not prevail only in Europe, but also in this country, where the moral treatment of the early 19th century—quite similar in many ways to modern forms of hospital treatment—suffered a severe setback.[42] Furthermore, the subdivision of Italy into many regions subject to different rulers and the natural isolation of Sicily contributed to the ignorance of Pisani's work on the part of other Italian psychiatrists.

The only memory of Pisani during that time was in Sicily, as evidenced by the foundation of the psychiatric journal *Il Pisani* in 1853. This journal was discontinued after about ten years, but has reappeared from 1880 up to the present time as the official journal of Sicilian psychiatrists.[43] In the meantime, in 1879, Pisani's biography by the psychiatrist Bernardo

[39] On the last days of Pisani's life and on his death, see the inspiring pages written by A. Di Giovanni. *La vita e l'opera di Giovanni Meli.* Firenze, Le Monnier, 1934, pp. 247-250.

[40] Linares, *op. cit.*

[41] Serio, *op. cit.*

[42] C. B. Farrar (ed.) Centennial Anniversary Issue, *Am. J. Psychiat.*, 1944, *100*: i-v, 1-199; J. H. Hall, G. Zilboorg and H. Bunker (eds.) *One Hundred Years of American Psychiatry.* New York ,Columbia Univ. Press, 1944; J .S. Bockoven. "Moral treatment in American psychiatry." *J. Nerv. & Ment. Dis.*, 1956, *124*: 167-194, 292-321.

[43] G. Padovani. *La stampa periodica italiana di neuropsichiatria e scienze affini.* Milano, Hoepli, 1946.

Salemi-Pace, appeared, a well-informed and objective contribution of considerable value.[44]

The same year, the German psychiatrist Eduard Wilhelm Güntz published in Leipzig a monograph on Pisani, which still remains a basic contribution. As previously mentioned, Güntz, born in 1800, became ill in Palermo while on a tour to European mental hospitals during the years 1827-1829 and was treated by Pisani like a son. Later on, in 1839, Güntz founded a private mental hospital in Thonberg, near Leipzig, which he directed until 1863.[45] The memory of Pisani must have remained vivid in Güntz's mind for fifty years, as a year before his death he finally decided to describe Pisani's institution in a book, intended to defend Pisani's priority over Conolly.[46] The book itself,[47] as is evident from the frequent warm expressions of gratitude and admiration, was conceived by Güntz as a tribute to a beloved teacher and guide. Its historical value remains very high, however, because of the complete translation of Pisani's *Regulations* (*Istruzioni*), which offers the only direct source of Pisani's ideas to the modern reader.

Güntz's monograph, unfortunately, remained virtually unknown to psychiatrists and medical historians. Pisani's name is not mentioned, in fact, in any book on the history of psychiatry, even by authors who dedicated extensive studies to 19th century psychiatry, like F. Lentz [48] and E. Kraepelin.[49] It is therefore surprising to find a detailed description of Pisani's ideas in a recent German book on psychiatric treatment by Carl Schneider,[50] where Pisani's emphasis on keeping patients occupied in

[44] Salemi-Pace, *op. cit.*

[45] For the biographical data on Güntz, see: H. Laehr. *Gedenktage der Psychiatrie.* Berlin, Reimer, 4. ed., 1893.

[46] John Conolly (1794-1866), physician of the Hanwell Asylum in Middlesex, England, from 1839 to 1843, is officially considered the strongest supporter of the "nonrestraint" system. His ideas became especially well known after the publication of his book, *The Treatment of the Insane without Mechanical Restraints.* London, Smith, 1856.

[47] The full title of this monograph is: *Don Pietro Pisani, der Vorläufer John Conollys.* Eine Gratulations-Novelle zur Feier des 25. Jahrestages der Promotion des Herrn Dr. med. Julius Maximilian Theobald Güntz am 22. März 1878, Direcktors und Administrators der Irren-Heil und Pflegeanstalt Thonberg bei Leipzig, geschrieben und dargebracht von Dr. Edward Wilhelm Güntz, senior, K. S. Geheimer Medicinalrath. Leipzig, Reklam, 1878. For a review of this monograph, see: *Il Pisani, Gazzetta sicula di freniatria,* 1880, pp. 168-174. Previously, in 1828, E. W. Güntz had published a short memorial on Pisani's institution under the title: "De hospitio dementium panormitano cogitationes." (See Serio, *op. cit.*, p. 83).

[48] F. Lentz. *Histoire des progrès de la médecine mentale depuis le commencement du XIX siècle jusqu'à nos jours.* Gand, Vanderhaeghen, 1876.

[49] E. Kraepelin. *Hundert Jahre Psychiatrie.* Berlin, Springer, 1918.

[50] C. Schneider. *Behandlung und Verhütung der Geisteskrankheiten.* Berlin, Springer, 1939, pp. 32-33.

different ways is especially praised. This description, together with the one given by Carlo Ferrio in his history of psychiatry [51] are—as far as it is known—the only isolated references to Pisani's work in modern psychiatric literature.

Pisani's work terminated with his death,[52] and his method of treatment —in spite of the admiration of a few—remained peripheral to the great psychiatric revolution of the early 19th century. This fact was certainly not due only to fortuitous circumstances however important, like the epidemics of cholera in 1837. Rather, it has to be referred to historical and cultural factors of basic significance. This explains why his work cannot easily be compared to that of other reformers of the treatment of mental patients, who were active at the end of the 18th century and in the early decades of the 19th century. The work of Chiarugi, Pinel, W. Tuke, and Langermann was an expression of the urge of contemporary society toward social reforms. It is sufficient to recall the underlying social structure supporting the ideas advanced by these innovators, like the progressive attitude inaugurated by the Grand Duke Leopold I in Florence, the social reforms brought about by the French revolution, and the humanitarian atmosphere introduced by the Quakers at the York Retreat in England.

As above mentioned, no matter what could have been the direct influences which motivated Pisani to initiate his reform, culturally and historically Sicilian society of Pisani's time still remained largely at a feudal stage. The king, considered as a god-like figure on the one side, and the despotic barons on the other side, were still the polar forces toward which the largely ignorant and superstitious poor inhabitants of the island alternately moved. This is the reason why Pisani's work, not a direct expression of environmental forces like that of the other reformers, remains somehow different from them as an isolated phenomenon, in spite of the common humanitarian urge.

Pisani's institution, indeed, is understandable—at least to a great extent —as an expression of the feudal society of Sicily. Pisani presents himself as a great, wealthy man, protected by the king, who opens the doors of his magnificent house—a villa surrounded by a marvellous park rather than an institution—to the poor and the sick. The nurses acted as his servants rather than his co-workers. Furthermore, not only the official

[51] C. Ferrio. *La psiche e i nervi. Introduzione storica ad ogni studio di psicologia, neurologia e psichiatria.* Torino, Unione Tipogr. Editr. Torinese, 1948, pp. 376-378.

[52] Marmont's wish, expressed by him to a friend in 1835, that Pisani should try to find a successor worthy of him, in order to prevent the disappearance of the institution he had established, remained unfortunately unfulfilled. (Serio, *op. cit.*, p. 107).

direction of the institution, but—what is more important—personal contact with the patients, was all centered on Pisani himself. There is no evidence, in fact, from Pisani's biographers, of anyone directly influencing the patients other than Pisani himself. If one considers also the fact that Pisani started to work with patients at 64 and that at that time he was already a well-known venerable figure, it is no wonder that a legend was built around him.[53]

Probably, an important if not necessary factor for the formation of this legend was the particular suggestibility of the Sicilian population, as evidenced by many traditional aspects of the local folklore. It is worth pointing out, however, that his patients were not hysterical personalities, but frankly psychotic individuals, as clearly appears from some of the descriptions, so that the element of suggestion alone could not explain the success of the treatment.

Independently from the pathology of the mental patients, the cultural element remains nevertheless important, if considered in the context of the other Mediterranean cultures. It is interesting to observe, incidentally, the similarities between Pisani's approach to mental patients and that employed in some other Mediterranean countries in the past, a fact which could be explained on the basis of common cultural and historical influences.[54]

[53] From the above mentioned article of the Swiss newspaper, *Le Fédéral,* it appears that a physical contact with Pisani, even a simple shaking of hands, was highly sought by mental patients. Such an approach carries some similarities with the medieval tradition of the so-called "royal touch," by means of which it was believed that certain diseases could be cured by the imposition of the hands by the king. This practice, which is reported in detail by many medical historians (especially by F. H. Garrison. *An Introduction to the History of Medicine.* 4. ed., Philadelphia, Saunders, 1929, p. 288, and by D. Guthrie. *A History of Medicine.* Philadelphia, Lippincott, 1946, pp. 209-211), was applied even to psychological disorders (W. Bromberg. *Man Above Humanity. A History of Psychotherapy.* Philadelphia, Lippincott, 1954, pp. 36-37).

[54] As a typical expression of these influences, it is worthwhile to recall the mental hospital of the Turkish city of Adrianople. This institution,—as described by the chronicler Eviljia in 1651 (see the translation of his report in *Quellenbeiträge zur Geschichte islamisher Bauwerke*, edited by C. H. Becker, Strassburg, 1912, and quoted by J. E. Stahelin. "Zur Geschichte der Psychiatrie des Islam." *Schweiz. med. Wchnschr.*, 1957, *87*: 1152)—founded by the Sultan Bajezid II (1481-1512), consisted in the 15th century, of a large dome-like octagonal building, divided into winter and summer quarters. According to Eviljia, this building was surrounded by a paradisiacal park, containing a garden of roses, orchids, vineyards, and many little fountains and ponds, alternating with waterfalls. To induce relaxation, the patients were made to walk under the flower-covered arbors (the typical oriental theme of the importance of perfume!) and to listen to melodious compositions played by musicians accompanied by singers. Although it is not known how many patients were treated in this way and how many improved, it is certain that all kinds of people were accepted there, poor and wealthy, young and old.

No matter how significant these similarities are, even more striking are those between his work and that carried on with some mental patients of more advanced countries around the world. The social differences between more progressive and more backward countries, suggested above, could not completely overshadow the common *Zeitgeist* of humanitarianism and liberalism, that came to its full and dramatic expression with the War of Independence in this country and the French revolution in Europe. The new spirit of social and political equality was manifesting itself in the work of many people, even in some still subjected to feudal governments.

Perhaps still under the influence of the idea that the study of mental disturbances did not belong necessarily to medicine,[55] many laymen around the same decades responded enthusiastically to this humanitarian urge toward mental patients. Moral treatment was the common theme which unified all these people of different cultures and traditions, from Rush, to Pinel, to Chiarugi, to the Tukes, and to many others. Similarities in their writings and in their approach to mental diseases are quite obvious, as has been pointed out by several historians of psychiatry either in this country or in Europe.[56] In the United States—in line with the remarkable tradition of the York Retreat established by the Tukes in England—some of the most important early mental hospitals, private or supported by states (as the New York Hospital, Bloomingdale Division, up until 1825 and the mental hospital of Williamsburg, Virginia, up until 1841),[57] were cared for by laymen. Among the most well-known representatives of them were Thomas Eddy in Pennsylvania, Horace Mann in Massachusetts, and the Galt family in Virginia.[58]

In Germany, in the early 19th century, under the influence of the romantic movement, many laymen—beginning with Johann Christian Hoffbauer—actively tried to treat mental patients in small private institutions or even at home, at times with success, as in the case of the poet Hölderlin.[59] In England, especially, the treatment of mental patients by

[55] Among others, I. Kant had stressed this point in his *Anthropologie* (1798).

[56] G. Zilboorg and G. W. Henry. *A History of Medical Psychology*. New York, Norton, 1941, Chap. 8: "The Age of Reconstruction."

[57] L. D. Ozarin, "Moral treatment and the mental hospital," *Am. J. Psychiat.*, 1954, *111*: 371-378.

[58] A. Deutsch. *The Mentally Ill in America*. New York, Columbia Univ. Press, 1949, 2. ed.

[59] Johann Christian Hoffbauer, professor of philosophy in Halle, left several books on mental diseases and on their treatment. The famous poet Hölderlin, already in an advanced stage of schizophrenia, improved considerably under the treatment of his devoted friend Isaac von Sinclair. Similarly, the minister of police of Hannover was successfully treated for a mental disturbance by Samuel Hahnemann, the founder of homeopathy.

laymen assumed historical importance because of the work of William Tuke and of his descendants at the York Retreat. By an unusual coincidence, William Tuke and Pietro Pisani became superintendents of mental institutions at the age of 64, after careers dedicated to public and private enterprises of a different nature, but always enlightened by an humanitarian spirit. The similarities between these two men become even more striking when the approach to mental patients applied at York is compared to that applied in Palermo.[60]

Even in regard to treatment, similarities are quite pronounced between Palermo's mental hospital and the contemporary ones, (e. g. the Hartford Retreat, which was also founded in 1824), in that the treatment was strongly centered around the person of the superintendent. There is ample evidence, from the literature, that this was the common trend of the time,[61] even if not as marked as in Sicily, where Pisani's personality was surrounded by an almost supernatural aura, as evidenced by some episodes reported by his biographers.[62] This aspect, if translated into the modern terms of relationship between psychiatrist and patient, could explain the beneficial effect obtained by this approach in many different institutions. Other more specific details of the technique of treatment as employed in Palermo, especially the system of rocking the patient in a hammock until he fell asleep, were not applied in any other institution. The value of this particular measure, viewed in modern psychiatric terms of regression and of libidinous gratification, cannot be overlooked and deserves a more thorough discussion than this simple mention in a paper of historical nature.

Beside this, the principles followed by Pisani in the organization of his institution can offer a valid explanation for the high percentage of improvements and cures obtained. These principles, unfortunately, were to be soon forgotten in the second half of the 19th century, when the dependence of psychiatry on neurology and the isolation of the mental patients from the active life of the community became universally accepted in psychiatric milieus. Today, after the general recognition of the value

[60] For the York Retreat, see: D. Hack Tuke. *Reform in the Treatment of the Insane. Early History of the Retreat.* London, Churchill, 1892; R. Semelaigne. *Aliénistes et philanthropes. Les Pinel et les Tuke,* Paris, Steinheil, 1912; *The Retreat York, Addresses given during the 150th Anniversary Celebrations,* William Sessions, York, Ebor Press, 1946.

[61] In this country, especially through the work of Eli Todd, Isaac Ray, Pliny Earle, Amariah Brigham, Samuel B. Woodward, John S. Butler, Thomas Kirkbride, and others.

[62] The author of the above-mentioned report of the Genevan newspaper *Le Fédéral* specifically states that Pisani considered himself "as a man in charge of a most valuable thing, that of gradually returning to the mental patients the judgment that they had lost."

of dynamic psychiatry, the principles of moral treatment are again becoming meaningful. In the light of the recent developments in the treatment of hospitalized mental patients, concepts such as "milieu therapy "and "therapeutic environment" have become very valuable ones in modern psychiatry and are in the process of determining a slow but significant change in the approach to mental diseases. The importance, to the patients, of the hospital community is currently emphasized, as it was in Palermo's hospital, with the therapeutic goal of giving security and responsibility to the patients.

From the same perspective, Pisani's work, neglected by official psychiatry and forgotten for more than a century, acquires today new validity and historical significance. As evidenced from the above, it has been generally represented as an isolated attempt made by a self-trained man who expressed his philanthropic urge by assisting and helping mental patients.

Today, after the experience of a century of psychiatry, this attempt—though an unusual expression of the Sicilian culture—can no longer be considered in these terms, but should rather be placed within the context of the other attempts made in the same direction in the Old as well as in the New World. In a way, some of Pisani's views are even more significant than those of the other contemporary outstanding philanthropists and scientists above mentioned, in that he anticipated some very modern concepts of the treatment of hospitalized mental patients.

To conclude, Morel's judgment of Pisani, an attempt to characterize the overall impact of Pisani's reform, remains actual and valid: Pisani "is one those men created by Divine Providence from time to time in order forcibly introduce ideas and useful reforms into human society." [48]

[48] B. Morel, "Pathologie mentale en Italie," *Ann. méd. psychol.*, 1846, *7*: 81.

THE DEVELOPMENT OF PHYSIOLOGY IN THE LAST FIFTY YEARS *

CHANDLER McC. BROOKS

Introduction

I think one would not have much difficulty defending the idea that the acquisition of knowledge and the development of sciences do not progress at a constant or uniform rate. There are sudden surges of progress of varied duration and then periods of relative quiescence. It is not reasonable to expect these periods of advance to coincide with the beginning of a century or any calendar date. Nevertheless one can usually find that developments have occurred within the span of a number of years, especially during the recent ages characterized by increased population growth, better communications, and accelerated pace of living. If one is not too meticulous about what dates are included in the " last fifty years " or in the " first half of this century," some very striking changes can be claimed for physiology within this modern era.

Development of a science can be said to consist of at least three components: 1) Development of method, instrumentation, skill and technique, 2) Acquisition of factual information and the generation of new fields or subdivisions of subject matter as an organizational consequence of this advance, and 3) The birth of new concepts or major ideas, and the growth, maturation, and extension of older insight. This latter process permits synthesizing thought, the appreciation of relative significances and the establishment of order from something which otherwise might be chaos.

These three processes do not occur independently and cannot be discussed completely separately. Dr. Cranefield and I will endeavor, however, to share responsibility for discussion of the developments of physiology in the first half of this century. He will concentrate his thought on the development of methodology, i. e. the use of methods and instruments permitting analysis of functional phenomena, and on the study of the ultimate structural and functional units of living matter. In contrast to this approach, I shall attempt to deal with the major concepts of

* Read at a symposium on " The Development of Physiology in the Last Fifty Years," thirty-first annual meeting of the American Association for the History of Medicine, New York, N. Y., May 22, 1958.

thought which have influenced physiologists in this last half century and which have permitted, and contributed to, the development of newer subject matters which may be considered subdivisions of physiology in its broader sense.

Physiological chemistry, endocrinology, biophysics, electrocardiography, electroencephalography, are among developments of this half century. Each has its society, its journals, its annual meetings and its language. A plethora of ideas, facts, and methods has created the seeming necessity to specialize and confine one's skills, interests, and knowledge to only a portion of the massive accumulation of publications and scientific observation. It may be that the development of physiology and its triumph will lead to its undoing. Is there any biological scientist who does not consider himself to be a physiologist? Is there any thought concerning living processes or tissues or living substance which does not now predominantly imply the notion of function? Perhaps this half century has seen the end of physiology as a discrete entity. This may be the last half century of physiology, but I have another idea which I will eventually present by way of conclusion.

Regardless of what our present state and our future may be, it can be said that there are a few major ideas which have characterized physiological thought, and these ideas have matured and have led to several developments during the past half century. It is now appropriate that I deal more directly with them and my specific subject.

Development of the Major Concepts of Physiology During the First Half of the Present Century

It is difficult to say just when physiology began. Certainly William Harvey's description of the circulation of the blood and function of the heart in the early 17th century, and Stephen Hales' measurements of blood pressure and calculations of cardiac output in 1732, were contributions to physiology.[1] Before this relatively modern time Galen, in the second century of our era, made contributions to physiology, and Aristotle, who was born in 384 B. C., wrote much about the function of organs and body parts. As a matter of fact, the Greek concept of balance and its importance has a striking resemblance to our modern concern with imbalance, the effects of stress, and the maintenance of homeostasis.[2] This merely indi-

[1] J. F. Fulton, *Selected Reading in the History of Physiology*. Springfield: Charles C Thomas, 1930.

[2] E. Hamilton, *The Greek Way*. New York: W. W. Norton & Co., 1930.

cates that the basic ideas of scientific thought have not always been generated completely within the framework of that discipline.

Thoughts of the origin of physiology and our recent contributions lead one to inquire—What was the state of physiology at the beginning of this century? By way of partial answer to this question a few occurrences can be emphasized: First, the death in 1894 of Hermann Ludwig Ferdinand Helmholtz who had, like Mayer and Joule, attained some appreciation of the conservation of energy,[1] who had measured the speed of conduction in nerve, who had proposed a theory of color vision, and who now is judged to have been one of the truly great physiologists. Karl Friedrich Wilhelm Ludwig, inventor of the kymograph, the mercury manometer, and one of the greatest physiologists of all time, died in 1895. Emil du Bois-Reymond died in 1896. The great Claude Bernard had lived until the last quarter of the past century. These and other of the great physiologists who had brought this science to a state of prominence and maturity, had ended their careers just before the beginning of our century. They left others no less distinguished who were just beginning to assume leadership in this field. Unquestionably, physiology had attained maturity and gained significant subject matter and direction.

Secondly, America had become productive. What is often referred to as the first significant contribution to physiology from this continent, William Beaumont's *Experiments and Observations on the Gastric Juice and the Physiology of Digestion,* had been published in 1833. There were, however, no physiologists on this side of the Atlantic able to supplement this work. It was in 1846 that Morton gave his demonstration of the efficacy of ether as an anesthetic, but a summary of experimental work in physiology done in America, published by Weir Mitchell in the *North American Medico-Chirurgical Review* 1858, showed that little had been accomplished here except by Dalton and Mitchell, and by Brown-Séquard in the course of his temporary residence in the United States. But soon thereafter (1861), Austin Flint was made Professor of Physiology in the Bellevue Hospital Medical College. In the late seventies, and almost simultaneously, physiology laboratories were established at Harvard Medical School under Bowditch, at the Graduate School of the Johns Hopkins University under Newell Martin, and at Yale University for Chittenden, although this latter laboratory, like that which was established by Vaughan in 1876 at the University of Michigan, was more properly a laboratory of physiological chemistry. Work had begun at Philadelphia, at the University of Virginia, and in other medical centers. On Friday,

[1] H. von Helmholtz, *Über die Erhaltung der Kraft.* Berlin: G. Reimer, 1847.

December 30, 1887, in the physiological laboratories of the College of Physicians and Surgeons, New York, the American Physiological Society was founded.[4] The original membership consisted of 28 persons. American physiology had been established by the students of Bernard, Ludwig, Michael Foster, and other of the great European physiologists already mentioned. They were supported by a new generation of men trained entirely in America, among whom were William Henry Howell and William Thompson Sedgwick. At the thirteenth annual meeting of the Society which was held in Baltimore in December of 1900, Walter B. Cannon, George H. Parker, and thirteen others were elected to the Society. Some of them are living today (P. M. Dawson and A. N. Richards). On these lists of early electees are the names of those who assumed leadership in the advances of our century which I am to describe today.

Thirdly, and finally, certain ideas had been advanced and certain fields of study started which foretold several of the principal developments which have occurred within this present century. I will mention these contributions from the past century as I describe what I believe to be the major themes of physiology during the past fifty years.

I have selected six areas I consider to be the most significant, but I have omitted some which might in the opinion of others be equally worthy of consideration. Some of these no longer attract the same interest they did formerly; other activities are at their peak, while still others are in their formative stages. This is possibly the time to point out that in physiology, as in other branches of science, some techniques permit significant accomplishment and then become no longer useful. Experience has also shown that certain approaches and fields of study, though long profitable, become exhausted. New interests and methods must be found. The first area of physiology which I will describe, provides an example of such changes which may occur in a half century.

1. *The Study of Energy Metabolism.*

Two ideas were basic to the development of this field of physiology. The first is the mechanistic concept, or the idea of man as a machine. This of course has influenced thought concerning other aspects of physiology, as illustrated by a recent new interest in the construction of automatons which perform like living organisms[5] and in the comparison

[4] *History of the American Physiological Society Semicentennial. 1887-1937.* Baltimore, 1938.

[5] J. Pfeiffer, *The Human Brain.* New York: Harper and Bros., 1955.

of the brain and the computer. This latter approach has been termed "cybernetics." [6] The second basic contributory idea was the concept of the "law of the conservation of energy," which indicated that energy input must be balanced by an energy output. Among the best reviews of the historical development of ideas of metabolism is one written by a member of your association and a major contributor to this program, Dr. George Rosen.[7]

Though in the late seventeen hundreds Lavoisier and Laplace had actually related combustion to respiration and measured heat production in an ice calorimeter, it was not until some hundred years later that income and expenditures of energy were measured: in dogs, by Rubner in 1894, and in man, by Atwater, Rosa, and Benedict in 1901. In these latter studies indirect and direct calorimetry were finally done simultaneously and found to be in agreement.

The concept of basal metabolism was formulated prior to 1900, and even the "law of surface area" was put forward by Rubner in 1883 and Richet in 1889. It can be said, however, that the long controversy between the proponents of the surface area basis for comparison of body heat production, and those believing in a body weight comparison of metabolic rates, was finally brought to a rather satisfactory though probably incorrect conclusion in our century. We now express body heat production in terms of calories produced per square meter of body surface per hour.

The direct calorimetry done by Graham Lusk and DuBois at the Russell Sage Institute of Pathology here in New York, and that performed by Benedict and Carpenter in Boston, practically concluded that chapter of physiology in our time. To be sure, gradient calorimetry is still in use at the Naval Medical Research Institute in Bethesda, and the direct measurements of heat production by smaller organisms and tissues has not waned in popularity.

If one glances through any textbook dealing with energy metabolism, the illustrations are of Benedict-Roth apparatus; they show charts for determining surface area prepared by DuBois, or Boothby and Sandiford, tables prepared by Carpenter or Lusk, giving the respiratory quotients and heat produced by metabolism of common food stuffs. Even the effects of disease and of endocrine disorders have been thoroughly restudied in the last fifty year period, and tables and graphs showing normal and abnormal variations have been prepared in abundance. The methods and

[6] N. Wiener, *Cybernetics*. New York: John Wiley & Sons, 1948.

[7] G. Rosen, The conservation of energy and the study of metabolism. In: *The Historical Development of Physiological Thought*. New York: Hafner Publishing Co., 1959.

standards required for clinical practice were generally available before the nineteen forties. Calculations of efficiency, work costs, metabolic requirements, have become standard practice in animal husbandry.

The modern problems of metabolism are largely those of intermediate metabolism or the study of the basic chemico-physical processes of cellular function. The physiological chemist rather than the physiologist is now the one who is primarily concerned.

One other development, arising in part from the study of metabolism, is the science of nutrition. Attracting the attention of physiologists at its origins and even at present, this science also belongs primarily to the chemist or to a person called a "nutritionist," and physiologists do not dare claim it as their own. However it may be classified, it is certainly an offspring of physiological thought and has undergone phenomenal growth during the past fifty years.

2. *The Physiology of Digestion.*

Although Spallanzani (1729-1799) and Réaumur (1683-1757) had evinced much interest in the digestive action of gastric juice, and Kirchhoff, in 1814, had observed the amylolytic properties of saliva, and de Graaf had cannulated the pancreatic duct and studied pancreatic juice before his scientific career ended in 1673, and even though in 1833 Beaumont had published his studies of Alexis St. Martin's digestive functions, it still can be said that our knowledge of digestion has been acquired chiefly during the past fifty years.

By 1899 Bayliss and Starling had studied the mechanical activity of the intestine and formulated the "law of the intestine." They discovered secretin in 1902, and the search for hormones of the digestive system was begun on that date. This in itself was a major contribution to physiology. Walter B. Cannon also had begun his investigations of the digestive system and, before 1900, had discovered the usefulness of roentgen rays in such studies. His major paper on "The movements of the stomach studied by means of the Roentgen rays" was published in 1898, but his other major contributions appeared later. His studies of "The acid control of the pylorus" were published in 1907; his book on *The Mechanical Factors of Digestion* appeared in 1911, and the results of his work on hunger were published in 1912 and those on thirst in 1918.

Pavlov also began his studies of the digestive system before 1900, but the English translation of his monograph, entitled *The Work of the Digestive Glands,* was first made available in 1902, and again in 1910. Carlson's studies of *The Control of Hunger in Health and Disease*

appeared in 1916. Babkin's monograph on the secretory mechanisms of the digestive glands was first published in German in 1914. Alvarez's studies for the *Mechanics of the Digestive Tract* were carried on in the early nineteen hundreds and published in 1922, while the work of Ivy, Lim, and their associates, was done somewhat later.

In a brief summary such as this, all significant contributions to the study of the function of the digestive system cannot be mentioned. Among the most significant features have been contributions made to endocrinology, to conditioning, and to the physiology of learning. It appears that the claim to a dominating interest has considerably lessened. Studies of the processes involved in hydrochloric acid formation, of absorption and secretion, are still carried on rather actively, but without notable success of late. The physiological chemist is as much concerned as is the physiologist with the modern exploration of digestive functions. It can therefore be said that as in the case of energy metabolism, the first half of this century has been a period during which concern with digestive physiology attained a peak and then diminished in relative importance, partially because of the earlier successes.

3. *The Study of the Integrative Function of the Nervous System.*

The concept of excitability is a very ancient one, and it must have been obvious that activity of the body and its parts could be controlled to a degree by the application and removal of stimuli. When in 1845, in an obscure Italian Journal, *Annali Universali di Medicina,* edited by Annibale Omodei of Milan, the Weber brothers published their discovery of a truly inhibitory nerve, a completely new possibility could be visualized: namely, the interaction between excitation and inhibition to control body activity.

Step by step throughout the latter part of the nineteenth century the framework for the neurophysiological advances of our time was laid. A greater understanding of reflex action was made possible by discovery of the sensory and motor roots by Magendie (1822) and Bell, and by the observation of Herbert Mayo (1823) that action through isolated brain and spinal centers can occur. Marshall Hall also reported in 1833 the feedback of the effects of a stimulation to the part stimulated and discussed the reflex function of the medulla oblongata and medulla spinalis. This is the background for the work of Sherrington. He was already studying the antigravity response in 1898, but early in the nineteen hundreds he began to work on a series of problems which were of even greater significance. In 1904, he published a paper entitled " Corre-

lation of reflexes and the principle of the common path." In 1906, there appeared an article, " On the proprioceptive system, especially in its reflex aspect," and his Silliman Lectures—*The Integrative Action of The Nervous System*. This monograph and subsequent works, such as *The Reflex Activity of the Spinal Cord,* have become classics of physiology. Among his associates at this time was J. C. Eccles, who has carried on this research on the integrative function of the nervous system and of central synaptic activity until the present time.[8,9] John Fulton, another Fellow of Magdalen College, Oxford, has made significant contributions to this major field of physiology.[10]

The contribution of the Sherringtonian School to our understanding of the integrative functions of the nervous system has been one of the most significant advances of physiology in this century. Sherrington's analysis of the mechanisms involved in the antigravity responses of animals (decerebrate rigidity), originally set forth in 1898, forms another of the milestones of modern physiology. He probably was aided by Hughlings Jackson's concept of " release," but he deserves credit for initiating most of the neurophysiological studies of significance which have been concerned with postural reactions. The investigations by Magnus of postural reflexes were begun in Sherrington's laboratory at Liverpool in 1908. Subsequently Magnus, with deKleyn, Dusser de Barenne, Rademaker, and others, carried on these studies so well described in his *Körperstellung,* published in 1924.

Sherrington was also involved in the initiation of other neurophysiological projects which have made significant advance in the past half century. While a pupil of Sherrington's at Liverpool, Harvey Cushing assisted in the earliest attempts to delimit the motor areas of the cerebral cortex in the higher apes. In 1909, Cushing published " A note upon the faradic stimulation of the postcentral gyrus in conscious patients." It is well known that Fritsch and Hitzig (1870) had already defined the motor area of the brain in lower forms and that in the following years Ferrier, as a result of ablations and clinical observations, had established the localization of the motor cortex very much as we now know it. In the last twenty years, however, more refined stimulation experiments [11] and

[8] J. C. Eccles, *The Neurophysiological Basis of Mind.* Oxford: Clarendon Press, 1953.
[9] J. C. Eccles, *The Physiology of Nerve Cells.* Baltimore: The Johns Hopkins Press, 1957.
[10] J. F. Fulton, *Physiology of the Nervous System,* 3rd Ed. New York: Oxford Univ. Press, 1949.
[11] W. Penfield and T. Rasmussen, *The Cerebral Cortex of Man.* New York: The Macmillan Co., 1950.

use of the evoked potential technique for localizing sensory areas have permitted the discovery of a degree of cortical localization unanticipated by those who initiated these studies.[13]

It certainly would not be proper to end a discussion of neurophysiology in the first half of our century without reference to the use of conditioned reflex studies by Pavlov.[13] He clearly elucidated the role of conditioned responses in the function of the digestive system, but the implications of this phenomenon for the problem of learning have also had a profound influence on scientific thought, particularly in his own country during the last thirty or more years.

4. *Discovery of the Humoral Transmission of the Nerve Impulse.*

This advance in physiology is of such recent date that probably you are all familiar with the advent of these studies which will be only briefly summarized. It is now known that at all peripheral junctions between neurons acetylcholine release is primarly responsible for transmission of the impulse across the synaptic barrier. At junctions between nerve and muscle acetylcholine, norepinephrine, or epinephrine serve as mediators. The postganglionic parasympathetic fiber mediator is cholinergic, while adrenergic mediators transmit sympathetic signals to effector cells in most instances. These same mediators appear to be involved in transmission at some central synapses but not all. The search for other central nervous system mediators is at the present moment one of the principal interests of neurophysiologists and pharmacologists. Seretonin, amino acid derivatives, histamine, and various other substances, are under study as possible central synapse transmitters, but this is a development of the present moment and not of past years.

In considering this new subject it can first be stated that du Bois-Reymond, in 1877, suggested that somatic nerves activate skeletal muscle by either an electrical or a chemical process. The electrical concept became dominant for various reasons, but fifty-four years later, in 1921, Otto Loewi,[14] Cannon and Uridil,[15] and Dale [16] produced convincing evidence

[13] P. Bard, Studies on the cortical representation of somatic sensibility. In: *The Harvey Lectures*, Baltimore: Williams and Wilkins, series XXXIII, 1937/1938, p. 143.

[13] I P. Pavlov, *Conditioned Reflexes*. Oxford: Oxford Univ. Press, 1927.

[14] O. Loewi, Über humorale Übertragbarkeit der Herznervenwirkung. I. Mitteilung. *Pflügers Arch. f. d. ges. Physiol.*, 1921, *189*: 239.

[15] W. B. Cannon and J. E. Uridil, Studies on the conditions of activity in endocrine glands. VIII. Some effects on the denervated heart of stimulating the nerves of the liver. *Am. J. Physiol.*, 1921-22, *58*: 353.

[16] H. H. Dale, *Adventures in Physiology*. London: Pergamon Press Ltd., 1953.

of the operation of humoral transmission in the parasympathetic and sympathetic systems of nerves and at the skeletal muscle fiber endplate.

The factors contributing to the discoveries of these three men, Cannon, Dale, and Loewi, have been discussed elsewhere.[17] It suffices to say here that Elliott in 1905, on the basis of the observed similiarity between the action of sympathetic nerves and epinephrine, suggested that sympathetic impulses might act on smooth muscle by releasing minute amounts of an epinephrine-like substance at the nerve endings. There had been similar forecasts of the role of acetylcholine as a mediator of tissue responses. Hunt and Taveau in 1906 showed that acetylcholine had a marked effect on blood pressure, that it dilated blood vessels, and that it and/or other choline derivatives were present in tissues.

It is now realized that both electrical and chemical processes are involved in transmission of the integrating actions of the nervous system. The transmitter agents are released at the nerve terminals and act upon the postsynaptic membranes to generate activity in these effector cells. Although this idea of humoral mediation is old, knowledge of the nature of transmitter agents was not obtained until the first half of our present century.

5. *The Development of Endocrinology.*

Long before the beginning of the 20th century much of the knowledge and many of the ideas of endocrinology were present. The concept that humours travel through the body influencing emotional states and producing reactions is very old. Organotherapy was employed in China in ancient times and accepted as a proper procedure by Paracelsus (1493-1541). There were several factors, however, which retarded development of this field until the beginning of the nineteen hundreds. Little progress could occur until assay methods were devised or until advances were made in other sciences, particularly in the fields of protein and steroid chemistry.

The first hormone was isolated and named by Bayliss and Starling in 1902. The early discovery of the digestive system hormones was relatively easy because the digestive system served as a test object.[18] Secretin,

[17] C. McC. Brooks, Discovery of the function of chemical mediators in the transmission of excitation and inhibition to effector tissues. In: *The Historical Development of Physiological Thought, op. cit.*

[18] C. McC. Brooks and H. A. Levey, Humorally transported integrators of body function and the development of endocrinology. In: *The Historical Development of Physiological Thought, op. cit.*

gastrin, pancreozymin, enterogastrone, enterocrinin, cholecystokinin are among the hormones of this group now recognized.

A full quarter of the thirty or so hormones now identified are directly concerned with development of sexual characteristics and with the phenomena of reproduction. Knowledge of the function of the sex glands cannot be claimed as modern. Xenophon (430-355 B. C.) wrote about the effects of castration; Théophile de Bordeu in 1775 correctly described male hormone function, and Berthold in 1849 demonstrated its existence. Eighty-six more years were required, however, before the male sex hormone was isolated and analyzed. This was accomplished by Laqueur, Butenandt, and others from about 1930 to 1935. The steroid chemists were then able to deal with the problem of isolation and identification of this and similar compounds.

The female sex hormones were also known to exist long before they were isolated and identified. Crystalline estrone was prepared in 1929 and estriol was isolated in 1930. During the following decade these materials were studied and finally synthesized. In 1929, Corner and Allen devised a simple bioassay technique for luteoid materials and soon thereafter crystalline corpus luteum hormone was isolated by Hisaw (1930-32) and progesterone was prepared by Butenandt in 1934.

Another category of hormones includes those which are primarily concerned with metabolic processes. The discovery of insulin and the study of its role in carbohydrate metabolism began in the early twenties although a good deal had been learned about the function of the islets of Langerhans and diabetes mellitus before that time. Abel isolated epinephrine from the adrenal medulla in 1899 and crystalline preparations of the naturally occurring l'adrenaline were obtained in 1901. Cannon's long continued studies of the function of this compound were summarized in monographs published in 1929, 1932, 1937. The study of adrenal cortical function was initiated by Addison in 1849 and continued intermittently until, in 1930, active extracts of cortical materials were obtained by both Swingle and Hartman. By 1936 several crystalline products had been obtained by Kendall, Reichstein, and others. The first adrenal steroid to be synthesized was 11-desoxycorticosterone and this was accomplished by Steiger and Reichstein in 1937. Determination of the role of these compounds in the body economy has been one of the major interests of physiologists and clinicians for some time. The thyroid too has attracted much attention during the past fifty years, although more knowledge of its functions was available than of the adrenals before 1900. In 1915 Kendall isolated from thyroid tissue a crystalline substance,

"thyroxin," which possessed high thyroid activity, and in 1926 Harington reported its structural composition. The history of the search for the active thyroid hormone has been dramatic and the story is still incomplete. The parathyroids and other glands might also be mentioned. What is known of their actions has been obtained in this century.

Little will be said of the remaining family of hormones, those liberated from the hypophysis. The tropic and other hormones produced by the various lobes of this gland have all become known during the period with which we are dealing. Thyrotropic, adrenotropic, and gonadotropic hormones influence the activity of other endocrine glands and a feed-back mechanism controls their output. Growth hormone, posterior lobe hormones, intermedin, lactogenic hormone etc., act directly upon effector cells and various mechanisms of control have been suggested. Most of the information concerning function of these hormones and the role of the hypophysis as an integrator of endocrine controlled behavior has been obtained in the past fifty years.

Hypothalamico-hypophyseal relationships have recently come under intensive study, and it is felt that in the near future a better understanding will be achieved of those mechanisms which operate to integrate the activities of the two systems controlling body function, i. e. the nervous and the endocrine systems.

6. *The Study of Homeostasis.*

In discussing the development of physiology during the past fifty years I have referred specifically to fields of study which have, of course, been the outgrowths or consequences of ideas and technical progress. In conclusion I wish to deal with a concept which has affected physiology in the past and also in our present era.[19]

One might trace the basic idea of homeostasis back to the Greeks because they certainly appreciated the necessity of balance and maintenance of a degree of constancy in life. The more scientific expression of this thought was given by Claude Bernard when he pointed out that the cells of the body live in a constant environment, and that this constancy is essential if they are to survive or even maintain a reasonably normal function.

Walter B. Cannon employed the term "homeostasis" and, in 1932, published his monograph entitled *Wisdom of the Body,* which is primarily

[19] L. von Bertalanffy, Modern concepts on biological adaptation. In: *The Historical Development of Physiological Thought, op. cit.*

concerned with description of the constancy of body states and the reactions maintaining them.

One of our modern ideas concerning body physiology is that body reactions can be subdivided into three categories; 1) reflex or voluntary postural and phasic responses, 2) reactions designed to maintain a constancy of the internal environment, and 3) adaptive reactions which adjust body functions to better meet the requirements imposed by the changing environment. If these last two adjustments are too difficult to accomplish, physiological strain occurs. The resulting stress is of considerable importance.[20]

Selye has been among those most interested in reactions of the body during stress. This notion has been popular for a number of years, and a vast amount of work has been done to determine the role of the adrenal cortex, the kidney, and other body organs in this type of reaction. The study of the response to stress and of recuperative reactions is a current phase of this general concept under discussion.

Conclusion

I have said nothing about studies of blood, the anemias and blood clotting, nothing about the discovery of vitamins, and studies of enzyme systems, because these are now within the sphere of influence of physiological chemistry. I have not mentioned studies of emotional expression and the developments of what might be called physiological psychology. Practically every branch of physiology has advanced to a significant degree, and even after Dr. Cranefield adds to the list of things I have discussed, there will remain much of significance which has been unmentioned. There remains one final theme, however, which I wish to call to your attention by way of my conclusion.

Physiology, like all other areas of our cultural endeavor, has been affected by man's ventures into outer space and the technical advances which have begun to make their realization conceivably possible. Within this first half of the 20th century we have already seen the development of what has been called aviation physiology, and we have acquired new knowledge of high altitude effects on man. This has all pertained, however, to man in his terrestrial environment. But now a new day is dawning. Physiologists are asked to learn how a man can live in an earth satellite; how his functional limitations will prescribe the speed and nature

[20] H. Selye, The general adaptation syndrome and the diseases of adaptation. *J. Clin. Endocrinol.*, 1946, *6*: 117.

of the movement of rockets and of man-carrying projectiles; how man can live where there is complete weightlessness; how he can carry with him or create on the planets, and from the energy found there or obtained from the sun, an environment in which his life processes can continue to function. We stand here in the beginning of another half century boldly jesting but filled with apprehension. One thing is sure as time passes inexorably—and that is that before the dawning of another century man will attempt to invade space, the moons, and planets of our solar system. This endeavor most surely will provide another new and unique chapter in physiology's history. I predict new fields of physiological thought, and not its dissolution, in this new half century.

MICROSCOPIC PHYSIOLOGY SINCE 1908 * [1]

PAUL F. CRANEFIELD

In 1935 in *The Search*,[2] a little known, realistic, and somewhat bitter book about scientific research as a way of life, the now famous novelist C. P. Snow remarked that only two fields of study in physics seemed likely to be worthwhile in the future. Those, he said, were the study of the atomic nucleus and the study of the complex molecular systems which form the physical basis of life. Snow himself is a physicist and was in 1935 engaged in the study of the structure of complex molecules. His statement about the future of physics in 1935 was a statement which quite a few brilliant young men were making at that time. The study of the atomic nucleus had results with which we have all acquired a modest familiarity. It created the Atomic Age, which began in 1945 and exerted a considerable influence over men's thinking during its brief life span so dramatically terminated by the advent of the Space Age.

Snow's alternative for the bright young physicist, the study of the complex molecular processes which form the substructure of life, has yet to create the Age of Biophysics, but it has inspired enough interest to lead to formal recognition in terms of a scholarly society. The Biophysical Society was organized in 1957 in Columbus, Ohio, and formally voted into existence in Cambridge, Massachusetts, in 1958. Biophysics will prove to be an important part of the area of microscopic physiology which I am to survey.

In planning these two lectures Dr. Brooks [3] and I decided to leave in my hands an analysis of advances in studies of the cell, and of smaller

* Read at a symposium on "The Development of Physiology in the Last Fifty Years," thirty-first annual meeting of the American Association for the History of Medicine, New York, N. Y., May 22, 1958.

[1] In this article I necessarily make many references to specific scientific studies. In no case should it be assumed that the study referred to is the first of its kind or even the most important. I have chosen examples which are familiar to me and which are readily accessible. In some cases I have referred to reviews or monographs. It also must not be supposed that my choice of examples is comprehensive. A well balanced survey of the field which I am examining can be found in Hugh Davson, *A Textbook of General Physiology*. London: J. & A. Churchill, 1951.

[2] C. P. Snow, *The Search*. Indianapolis and New York: Bobbs-Merrill Company, 1935, pp. 186, 187.

[3] Chandler McC. Brooks, The development of physiology in the last fifty years. *Bull. Hist. Med.*, 1959, *33*: 249-262.

units which are not in themselves alive but which are organic in the sense that they compose living cells and in general can be obtained only from living cells. Such studies I propose to call microscopic physiology. The term is useful in its analogy to microscopic anatomy, and indeed the majority of studies I will mention depend in part upon the use of the microscope, either in making the experimental preparation or in carrying out the experimental procedures. We might, less seriously but not completely frivolously, interpret microscopic physiology as microphysiology and micro- as the one millionth part. If we choose to regard a 70 kilogram human as the unit, then microscopic physiology deals with experimental preparations weighing 70 mg or less (much less in general, as in the study of a single muscle fiber weighing perhaps 0.1 mg). Even at this level of biological analysis a clear distinction appears between the study of preparations made up of one or more intact cells and the study of molecules and molecular aggregates which make up cells and are obtained from them. The study of such molecules and molecular aggregates has been aptly designated "molecular biology."

The most obvious example of sub-cellular units are the now familiar enzyme systems. A consideration of those systems brings me directly to the beginning of the period assigned to us, namely, 1908-1958. It is arbitrary but convenient to state that in 1908 the subject we know as biochemistry had reached independence and maturity and was rapidly becoming a separate department of instruction in medical schools. This very important fact suggests that in asking me to speak on the history of physiology since 1908 you have deprived me of a very large and important area of discussion, the history of biochemistry since 1908. On the other hand, it seems likely that when, in 2008, another such symposium is held, it will be necessary to remark that the period under discussion began with the loss to physiology of another of its major subdivisions: biophysics. This seems like a sorry confession of failure: all that I can do is tell you about an epoch in the history of physiology in which the cellular and molecular approaches were so productive that they left home for good. But there is a paradox here. In spite of the defection of biochemistry in 1908, the average physiologist of today knows and uses far more biochemistry than did the average physiologist of 1908. Similarly, I venture to predict that the average physiologist of 2008 will know and use far more biophysics than does the average physiologist of today. A glance, therefore, at general and cellular physiology and biophysics during the last 50 years will acquaint us with fields which will have an ever-increasing influence on physiology either as parts of that science or as independent disciplines.

I will discuss at some length an area with which I am quite familiar, the history of studies on single muscle and nerve cells. I will then review some single unit studies on other types of cells and organs and attempt briefly to indicate the recent history of General Physiology and Biophysics.

Excitable Cells and the All-or-None Law

The earlier history of studies of single cells is closely linked with the "all-or-none" law, which was proposed for the heart by H. P. Bowditch in 1871. Bowditch's own statement of this law[4] is clearer than many made subsequently so I will give it in translation from the German original: ". . . the stimulus either evokes a contraction or it is unable to do so; and if it is able to do so it evokes exactly the maximum contraction which any stimulus can evoke at that instant."

The heart obeys the all-or-none law because its many fibers are functionally continuous so that excitation of any of them results in excitation of the entire heart. It is in this sense that the heart is said to behave like a single fiber. The problem of the all-or-none law is greatly complicated in a nerve or skeletal muscle of many fibers, since the size of the action potential or the strength of contraction might vary either because the response of each cell is variable or because the number of cells responding is variable. Since the way in which variable nervous activity is reflected in nerve fibers is of the utmost theoretical importance, the question of whether the all-or-none law applies to tissues other than the heart assumed a central position. The problem could be resolved only by showing that the single fiber did or did not obey the all-or-none law, and thus a powerful impetus was given to research on the excitation and response of single muscle and nerve cells.

Ingenious experiments by Keith Lucas are generally regarded as demonstrating that the contraction of single muscle fibers is subject to the all-or-none law.[5] Lucas used a muscle containing only a few fibers and was able to show that the strength of contraction of the whole muscle did not vary continuously but in discreet jumps and that the number of jumps might equal but never exceeded the number of fibers. Thus the variation in strength of contraction of the muscle depended upon some of its individual fibers contracting fully and some not at all.

[4] H. P. Bowditch, Über die Eigenthümlichkeiten der Reizbarkeit, welche die Muskelfasern des Herzens zeigen. *Berichte d. k. Ges. d. Wiss., Leipzig*, Math.-Phys. Cl., 1871, *2*: 652. (p. 687).

[5] Keith Lucas, The 'all or none' contraction of the amphibian skeletal muscle fibre. *J. Physiol.*, 1909, *38*: 113.

The death of Lucas in the first World war did not destroy the continuity of development of his ideas since his young associate, Edgar D. Adrian (now Baron Adrian of Cambridge), continued similar studies. A series of classical papers by Adrian and his collaborators (in particular Detlev W. Bronk)[6] succeeded in establishing the validity of the all-or-none law for motor and sensory nerve fibers. This work was done by cutting or damaging the fibers of a nerve until only one fiber remained functional. It could then be shown that increased activity in a nerve fiber results from an increase in the frequency of similar impulses rather than from an increase in the amplitude of the impulse. This again represented a demonstration of the all-or-none law for the single nerve fiber.

Midway in the period we are reviewing, the investigation of the all-or-none law had succeeded in showing that it applied to the contraction of single muscle fibers and to the action potential of single nerve fibers. In the mid-thirties a new approach to the single nerve cell appeared. J. Z. Young, having rediscovered the giant axon of the squid, called it to the attention of the physiologists [7] and initiated a remarkable series of developments in neurophysiology and electrophysiology. The giant axon of the squid is so large (up to 1 mm. in diameter) that it is comparatively easy to insert an electrode inside it. It is hard, perhaps, to see why recording electrical activity from the inside instead of the outside of a single cell should have any revolutionary consequences. Nevertheless it did. This came about in two ways. Firstly, the precision introduced into measurement of the action potential produced new problems and a new theory of the nature of the action potential which has been very influential.[8] Secondly, the realization that an electrode could be used inside a large cell led to attempts to record from ordinary cells with very small intracellular electrodes.[9] This new technique stirred the imagination of many, and as a result the last ten years have been a period of vigorous activity in electrophysiology. It has become commonplace to record from single skeletal muscle cells and possible, though difficult, to record from single

[6] A bibliography of this work is given in D. W. Bronk, The nervous mechanism of cardiovascular control. In: *The Harvey Lectures*, Baltimore: Williams and Wilkins, series XXIX, 1933/1934, p. 245.

[7] John Z. Young, Structure of nerve fibers and synapses in some invertebrates. In: *Cold Spring Harbor Symposia on Quantitative Biology*, Cold Spring Harbor, L. I., New York: The Biological Laboratory, vol. 4, 1936, p. 1.

[8] A. L. Hodgkin ,The ionic basis of electrical activity in nerve and muscle. *Biol. Rev. Cambridge Philos. Soc.*, 1951, *26*: 339.

[9] G. Ling and R. W. Gerard, The normal membrane potential of frog sartorious fibers. *J. Cell. and Comp. Physiol.*, 1949, *34*: 383.

cell-bodies in the central nervous system. A most remarkable achievement has been the recording, with microelectrodes, of the electrical activity of single end-plates of the myoneural junction (which do not, incidentally, obey the all-or-none law in any ordinary sense).

Thus the study of the single unit has progressed from the whole heart, unitary in its response to excitation, down to a structure as small as a single motor end-plate. In the whole development two ideas have been paramount: a study of the all-or-none law and a study of molecular mechanisms underlying conduction and contraction. Over and over again physiology has returned to the problem of the physical basis of motion and sensation, and the problem is as alive today as at any time in the past. There is a natural link between physiology and biophysics at this point since men interested in fundamental mechanisms of conduction and contraction have tended to be men of an analytical turn of mind interested in physics and chemistry and attracted to the study of the single unit because of its deceptive simplicity.

Other Single Unit Studies

The Heart: A new era in our understanding of the heart had begun by 1908. Einthoven's introduction of the string galvanometer made it possible to record the electrocardiagram accurately and easily. An enormous development in this field took place very rapidly, but single cell studies awaited the development of the Ling-Gerard microelectrode.[9a] The use of the intracellular electrode has provided a new understanding of many fundamental aspects of cardiac function. The action potential of every part of the heart has been examined, and in particular we have gained some understanding of the nature of the rhythmicity of the sino-atrial node and of the nature of the slow transmission of excitation through the atrio-ventricular node.[10]

Capillary: The techniques of Landis in which the movement of fluid

[9a] *Ibid.*

[10] The first published observations obtained by intracellular recording in the heart are found in E. Coraboeuf and S. Weidmann, Potentiel de repos et potentiels d'action du muscle cardiaque measurés a l'aide d'électrodes internes. *Compt. rend. Soc. de biol.* 1949, *143*: 1329. The results obtained up to July 1947 are reviewed in Paul F. Cranefield and Brian F. Hoffman, Electrophysiology of single cardiac cells, *Physiol. Rev.*, 1958, *38*: 41. Dr. Hoffman and I are completing a book on this subject. It will be about 400 pages long and will deal solely with studies of the heart obtained with intracellular electrode techniques during the last eight years. This rapid accumulation of knowledge is indicative of the general activity in the field of electrophysiology since the introduction of microelectrode techniques.

across a single capillary has been measured quantitatively,[11] have given wide confirmation to the basic hypothesis of capillary function advanced by Starling.

Kidney: The micropuncture method of A. N. Richards [12] has permitted analysis of the glomerular filtrate and of fluid in various parts of the tubule, all in a single nephron.

Muscle: The elastic and mechanical properties as well as the contractility of skeletal muscle have been examined in isolated single fibers.[13] The action potential of single muscle fibers has been measured with intracellular microelectrodes,[14] and the effect on it of many enzyme inhibitors and ions [15] has been determined. The flux of sodium and potassium in a single skeletal muscle fiber at rest and during activity has been determined with the aid of radioactive tracers.[16] The famous studies of the heat production of muscle, initiated by A. V. Hill, are still continuing and becoming increasingly delicate and accurate.[17]

Extensive studies on the submicroscopic structure of muscle have been made with the electron microscope.[18] Many conflicting results have been reported and many conjectures as to the structure and nature of the contractile protein have been formed.[19] Kinetic studies of certain chemical reactions have been carried out in intact muscle fibers.[20] Complex mathe-

[11] E. M. Landis, Capillary pressure and Capillary permeability, *Physiol. Rev.*, 1934, *14*: 404.

[12] A. N. Richards, Processes of urine formation. Croonian Lecture, *Proc. Roy. Soc., London s. B.*, 1938-39, *126*: 398.

[13] Ove Sten-Knudsen, *Torsional Elasticity of the Isolated Cross Striated Muscle Fibre. Acta Physiologica Scandinavica, 28*: Supplement 104, 1953.

[14] W. L. Nastuk and A. L. Hodgkin, The electrical activity of single muscle fibers. *J. Cell. and Comp. Physiol.*, 1950, *35*: 39.

[15] W. V. MacFarlane and J. D. Meares, Chemical modification of intracellularly recorded after-potentials of frog skeletal muscle. *J. Physiol.*, 1958, *142*: 78.

[16] A full report of these studies by P. Horowicz and A. L. Hodgkin has not appeared. It will no doubt appear in *The Journal of Physiology* in late 1958 or early 1959.

[17] This long series of studies on muscle heat has appeared and continues to appear in *Proc. Roy. Soc., London, s. B.*

[18] H. E. Huxley, The double array of filaments in cross-striated muscle. *Journal of Biophysical and Biochemical Cytology*, 1957, *3*: 631.

[19] D. R. Wilkie, Facts and theories about muscle. In: *Progress in Biophysics and Biophysical Chemistry*. New York: Academic Press Inc.; London: Pergamon Press Ltd., vol. 4, 1954, p. 288.

[20] Britton Chance and C. M. Connelly, A method for the estimation of the increase in concentration of adenosine diphosphate in muscle sarcosomes following a contraction. *Nature, London*, 1957, *179*: 1235.

matical models of the contractile process have been developed.[21] The electrical activity of single smooth muscle fibers has been studied.[22]

The Myoneural Junction: Direct measurements of the potential changes at a single motor end-plate,[23] in combination with microinjection of ions and drugs,[24] have enormously extended our knowledge of the way in which excitation is transferred from the nerve terminal to the muscle fiber.

Peripheral Nerve: The action potential of single nerve fibers has been measured and correlated with the fluxes of Na^+ and K^+ ions.[25] An intricate physicochemical and mathematical theory which unifies much of our knowledge about excitable tissue has been formed on the basis of this work.[26] The oxygen uptake of a few milligrams of nerve has been measured and the increase in oxygen consumption when those few milligrams of nerve conduct impulses has been measured.[27] This, incidentally, was done not long after Bayliss concluded that such an oxygen consumption did not exist, since all efforts to detect it had failed.[28] The heat produced by nerve as it conducts impulses has been measured.[29] The action potential of a single node of Ranvier is studied routinely today by electrophysiologists.[30]

[21] A. F. Huxley, Muscle structure and theories of contraction, In: *Progress in Biophysics and Biophysical Chemistry, op. cit.*, vol. 7, 1957, p. 255.

[22] E. Bülbring and H. Lüllmann, The effect of metabolic inhibitors on the electrical and mechanical activity of the smooth muscle of the guinea-pig's taenia coli. *J. Physiol.*, 1957, *136*: 310.

[23] P. Fatt and B. Katz, An analysis of the end-plate potential recorded with an intracellular electrode, *J. Physiol.*, 1951, *115*: 320.

[24] J. del Castillo and B. Katz, On the localization of acetylcholine receptors. *J. Physiol.*, 1955, *128*: 157.

[25] Hodgkin, *op. cit.*

[26] A. L. Hodgkin and A. F. Huxley, A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.*, 1952, *117*: 500.

[27] Frank Brink, D. W. Bronk, F. D. Carlson and C. M. Connelly, The oxygen uptake of active axons. In: *Cold Spring Harbor Symposia on Quantitative Biology, op. cit.*, vol. 17, 1952, p. 53. See also P. F. Cranefield, F. Brink and D. W. Bronk, The oxygen uptake of the peripheral nerve of the rat. *J. Neurochem.*, 1957, *1*: 245.

[28] William M. Bayliss, *Principles of General Physiology*. 4th ed. London: Longmans, Green, and Co., 1924, Chapter 13.

[29] T. P. Feng and A. V. Hill, The steady state of heat production of nerve. *Proc. Roy. Soc., London, s. B.*, 1933, *113*: 356.

[30] Important early work on the single node of Ranvier, the single nerve fiber, and the single nerve fiber-single muscle fiber preparation is reviewed in G. Kato, *The Microphysiology of Nerve*, Tokyo: Maruzen, 1934. A more recent book is I. Tasaki, *Nervous Transmission*, Springfield: Thomas, 1953. In the preface to this latter book Tasaki remarks "In . . . 1933 . . . it was certainly a great horror for the assistants . . . to

Sensory Receptors: The action potential of single fibers of the optic nerve has been recorded in both the invertebrate [81] and vertebrate eye.[82] The sensitive receptor cells have been examined individually with the aid of microelectrodes.[83] The visual pigments have been isolated, identified, and studied in detail.[84] Many other single receptor organs have been studied; e. g., single taste buds,[85] single Pacinian corpuscles,[86] and single muscle spindles.[87] The study of single muscle spindles has revealed the remarkable fact that the muscle spindle has a motor innervation and that the degree of tension and hence of sensitivity of the spindle is under reflex regulation.

Central Nervous System: Single cells have been studied electrically with intracellular electrodes.[88] Minute areas of cortex have been isolated and their metabolism measured: this has been done by cannulating blood vessels 25 *microns* in diameter.[89]

Glands: Electrical studies of single secretory cells have been carried out which suggest that the complex electrical response of the whole gland may eventually be explained in terms of the activity of its component cells.[90]

Ultramicroscopic Structure: The electron microscope and the methods

be given a suggestion . . . to work on isolated single nerve fibers." But, 25 years later, the technique is used by dozens of investigators as a matter of course.

[81] H. K. Hartline, Henry G. Wagner and E. F. MacNichol, Jr., The peripheral origin of nervous activity in the visual system. In: *Cold Spring Harbor Symposia on Quantitative Biology, op. cit.*, vol. 17, 1952, p. 125.

[83] S. W. Kuffler, Neurons in the retina: organization, inhibition and excitation problems. In: *Cold Spring Harbor Symposia on Quantitative Biology, op. cit.*, vol. 17, 1952, p. 281.

[82] There is some doubt whether records have been obtained from individual rods and cones. A recent consideration of the problem is given in E. F. MacNichol, Jr. and G. Svaetichin, Electric responses from the isolated retina of fishes. *Am. J. Ophth.*, 1958, *46*: 26.

[84] G. Wald, The chemical evolution of vision. In: *The Harvey Lectures, op. cit.*, Series XLI, 1945/1946, p. 117.

[85] L. M. Beidler, Properties of chemoreceptors of tongue of rat. *J. Neurophysiol.*, 1953, *16*: 595 .

[86] J. A. B. Gray and M. Sato, Properties of the receptor potential in Pacinian corpuscles, *J. Physiol.*, 1953, *122*: 610.

[87] C. C. Hunt, Muscle stretch receptors; peripheral mechanisms and reflex function. In: *Cold Spring Harbor Symposia on Quantitative Biology, op. cit.*, vol. 17, 1952, p. 113.

[88] L. G. Brock, J. S. Coombs and J. C. Eccles, The recording of potentials from motoneurones with an intracellular electrode. *J. Physiol.*, 1952, *117*: 431.

[89] P. W. Davies and A. Remond, Oxygen consumption of the cerebral cortex of the cat during metrazol convulsions. *A. Research Nerv. and Ment., Dis., Proc.*, 1946, *26*: 205.

[90] A. Lundberg, Electrophysiology of salivary glands. *Physiol. Rev.*, 1958, *38*: 21.

of X-ray diffraction have revealed a whole new level of subcellular organization. These studies are often carried out in close connection with physiological problems and there has recently been a revival of interest in the intimate bond between microscopic physiology and microscopic anatomy.[41]

All of these experiments which I have mentioned to you are exceedingly refined, elegant, and beautiful in technique, execution, and significance. All of them have been conducted by a group of men on whose mind the fascination of the ultimate units of life as objects of study has been compelling, men of the sort Adolf Fick said would enter biophysics because "of the attractive force which by its nature it must always exert on logical minds." [42]

General Physiology

The biophysics movement of 1847, which declined in importance rather rapidly at least as a program,[43] had an important successor in the movement known as General Physiology. The announced program of the biophysics movement of 1847 was the reduction of all vital processes to applied physics and chemistry. The announced program of the general physiologists was the study of those processes which are common to all living cells. The general physiologist became however more or less of a biophysicist or biochemist simply because the processes common to all living cells are physical or chemical in nature. Thus the emphasis on basic mechanism, and therefore on microscopic physiology, reappeared strongly around the turn of the century. It is well to point out that a tendency to use physical, chemical, and even mathematical methods in physiology does not suffice to identify a man of that period as a general physiologist. Thus in delivering this paper I referred to August Krogh as representative of general physiology, as indeed his interests would suggest. Subsequently, I have found the following remark by him: [44]

> The name does not matter much, though I confess that there is one name with which I have no sympathy,—that of 'general' physiology. I suspect that it is often used to denote just those aspects of a problem which are considered most

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[41] A number of reviews on ultrastructure are to be found in the volumes *Progress in Biophysics and Biophysical Chemistry*, edited by J. A. V. Butler and J. T. Randall, and B. Katz, which have appeared annually since 1950.

[42] Adolf Fick, Methoden and Richtungen der physiologischen Forschung. *Gesammelte Schriften*, Würzburg: Stahel, 1903, vol. 4, p. 389.

[43] Paul F. Cranefield, The organic physics of 1847 and the biophysics of today. *J. Hist. Med. and Allied Sc.*, 1957, *12*: 407.

[44] August Krogh, *The Progress of Physiology*, Address delivered at the opening of the XIIIth International Physiological Congress, Boston, 1929.

important from an individual point of view. In my opinion a general physiology which can describe the essential characteristics of matter in the living state is an ideal to which we may hope our successors may attain after many generations, and I want to emphasize that the route by which we can strive toward the ideal is by a study of the vital functions in all their aspects throughout the myriad of organisms.

This statement emphasizes the fact that general physiology must be identified by a program and viewpoint rather than by a set of methods and problems.

General physiology is identified to a considerable degree with Rudolf Höber, Jacques Loeb, and William Bayliss. Höber and Bayliss wrote textbooks which are perhaps unique in this century for their influence on physiology. Höber's *Physikalische Chemie der Zelle und der Gewebe*,[45] first published in 1902, progressed through many German editions. After Höber came to the United States he wrote, with the aid of collaborators, a new version of this book in English which remains in print years later as a standard work of reference and as a standard text.[46]

Sir William Bayliss' *Principles of General Physiology*[47] had a much shorter publishing career (four editions from 1915 to 1924), but it had a dramatic effect in the United States and England. "Bayliss Clubs" were formed by young physiologists to discuss the physical and chemical aspect of physiology emphasized by Bayliss,[48] and at least one Nobel Prize Winner (Dr. Herbert Gasser) has told me that the first edition of Bayliss' book exerted a powerful influence on him early in his career. If the first edition of Bayliss' book was important in turning Dr. Gasser's attention toward a physical and quantitative view of physiology, then it had an important influence indeed, since most of the electrical studies of single units depend upon the use of the cathode ray oscilloscope. The establishment of the cathode ray oscilloscope in physiology was the work of Dr. Joseph Erlanger and Dr. Gasser, and it was for this contribution and for the studies of the nerve action potential which they carried out with the cathode ray oscilloscope[49] that they were awarded the Nobel Prize.

[45] Rudolf Höber, *Physicalische Chemie der Zelle und der Gewebe*. 5th ed., Leipzig: Engelmann, 1922.

[46] Rudolf Höber, *Physical Chemistry of Cells and Tissues*. Philadelphia: Blakiston, 1945.

[47] William M. Bayliss, *Principles of General Physiology*. 4th ed. London: Longmans, Green, and Co., 1924.

[48] Obituary notice of Sir William Maddock Bayliss. *Proc. Roy. Soc. London, s.B.*, 1926, *99*: XXVII.

[49] J. Erlanger and H. S. Gasser, *Electrical Signs of Nervous Activity*. Philadelphia: University of Pennsylvania Press, 1937.

The final edition of Bayliss' *Principles* was revised by a group of men whose names also suggest the influence of this book: J. Gray, A. V. Hill, A. D. Ritchie, N. K. Adam, D. C. Henry, W. O. Fenn, A. J. Clark, J. C. Drummond, R. K. Cannon, E. H. Starling, G. V. Anrep, H. S. Gasser, E. D. Adrian, H. Hartridge, C. Lovatt Evans, E. F. Blackman, D. T. Harris, J. Barcroft, Thomas Lewis, H. H. Dale and A. E. Boycott.

Although Bayliss and Höber both were powerful and successful experimentalists their books assumed an even greater role in modern physiology than did their specific researches (excepting perhaps, Bayliss' role in the discovery of hormones). General physiology continues to be a recognized viewpoint and discipline, and it is too early to assess its history. We may say here that the early part of the period under review was characterized by a program of research which was very provocative and exciting and which, like biophysics, placed great emphasis on cellular and sub-cellular processes.

Biophysics

As stated in the introduction, The Biophysical Society was organized in 1957. This reemergence of biophysics nearly a century after the collapse of the 1847 program will undoubtedly be of great importance in the future. The ideas and even the name of biophysics (or medical physics) never disappeared, but the current movement in the United States has rather clear roots in the period beginning around 1920. It is noteworthy that the Biophysical Society deliberately avoided defining biophysics, partly to avoid an artificial limitation of the field, but mainly because no generally acceptable definition is available. Thus, at this moment in the United States, biophysics might be regarded as the collection of research interests represented by those persons who chose to join the society during the two year organizational period when membership was unrestricted. Thus defined, biophysics includes at least the following areas of study: the structure of macromolecules of biological origin; electrocardiography, muscle chemistry; muscle thermodynamics; muscle mechanics; sensory receptors; control theory; electrophysiology; the use of radioactive tracers; the effects of radiation on sub-cellular particles, cells, tissues, organs, organisms, and on longevity; mathematical models of sociological systems; ballistocardiography; oxygen metabolism of cells; electron microscopy; biological use of X-ray diffraction; biological luminescence; cell growth and division; whole organism mechanics and many other subjects. That this bewildering array of interests could be fused into a single scholarly society may seem unlikely; yet it is worth noting that at the first meeting

most participants felt that most of the papers presented were of interest to them and that many people they wanted to meet and hold discussions with were present. It is apparent therefore that a community of interest exists among those whose research activity is represented by the above list. The basis for this community of interest is, broadly speaking, that some physical, mathematical, or physical-chemical element is present in the theory or method applied to these diverse problems. This widely scattered but empirically linked group does not have an abstract program or viewpoint and thus contrasts sharply with the biophysics movement of 1847, and with the General Physiology movement. It includes, however, many people who work exclusively on cellular and sub-cellular problems and will undoubtedly have an increasily great influence in the area of microscopic physiology and molecular biology.

Microscopic Physiology and Medicine

Few of the men who created microscopic physiology in our time were ever intimately associated with and integrally part of a Medical School Faculty. Since we meet today as a History of Medicine Society I think it entirely appropriate that I should bring this out in the open. It is not exactly a scandal, but then again it is not exactly a good thing either.

I cannot enter into the broad question of the relation between medical science and biological research. That a drastic separation between pure research and the practice and teaching of medicine can have grave consequences has been well shown by Dr. Ackerknecht in a paper which should be carefully studied by anyone concerned with the future of scientific medicine.[60] It is only fair to remark that the results and methods developed in microscopic physiology have been rapidly absorbed by medical science. On the other hand I cannot address a Society for the History of Medicine on the subject of the History of Physiology since 1908 and conceal the fact that a whole vital and immensely productive division of physiology has had to exist on its own during that period.

I would therefore like to extend my subject somewhat and examine the relationship between the area of which I have spoken and Medical Science. If I now add biochemistry to the disciplines from which it separated so long ago the magnitude of the problem will become apparent. At a moment when the physician, the medical school, and the medical

[60] E. H. Acknerknecht, Medical education in 19th century France. *J. Medical Education*, 1957, *32*: 148.

administrator are under enormous pressure to enlarge their point of view and to become aware of the sociological aspects of medicine and of the psychological problems of the individual, medical and biological science is developing at a furious rate, and much of that development is occurring outside of medical schools. It may seem odd that I should touch upon this subject in connection with my talk to you. It forced itself on me. One cannot avoid it. It is an outstanding characteristic of research in the area I am examining.

Have the infinitely delicate and beautiful studies of microscopic physiology influenced the practice of medicine? By and large they have not. Will they some day? They must.

Biochemistry, biophysics, and general physiology during the last 50 years have attracted many of the young investigators best qualified by their analytical turn of mind and by their knowledge of physics and chemistry and mathematics to make fundamental contributions to our knowledge. Classical physiology, on the other hand, has drawn heavily on the medical school. Most classical physiologists are either M. D.'s or Ph. D.'s trained in a medical physiology department. Thus a gap has developed between microscopic physiology and medicine.

This gap has developed exactly because of the developments I have outlined to you. The steady success of applied medical research on the one hand, and the steady push of fundamental research into areas of less and less apparent applicability on the other hand, have created the illusion that there is such a thing as medical science which is comprised of medical physics, medical chemistry, medical anatomy, medical physiology, and medical bacteriology, and which is a body of knowledge sufficient unto itself, adequate to serve both for the practical foundations of medical practice and as a source of new discoveries, and thus self-contained and self-perpetuating.

This fallacious belief, which has the gravest possible consequences for the future of medicine, derives from the richness of the harvest which applied research in medicine is now reaping from the pure research of long ago. The medicine of the future can continue to reap such a harvest only if the medicine of today establishes a closer relationship with microscopic physiology than it has done during the last fifty years.

ANNOUNCEMENTS

AMERICAN ASSOCIATION FOR THE HISTORY OF MEDICINE, INC.

The Thirty-Second Annual Meeting of the American Association for the History of Medicine was held in Cleveland, May 21-23, 1959. The following matters were brought to the attention of the members.

Elections

John B. Blake, Secretary and Treasurer. Saul Jarcho, Esmond R. Long, Genevieve Miller, J. I. Waring, members of the Council to hold office for three years.

Upon nomination by the Council, Erwin H. Ackerknecht, M. D., Professor of the History of Medicine at the University of Zurich, Switzerland, was elected an honorary member of the Association.

Awards

The William Osler Medal was awarded to Mr. Richard L. Grant of the University of Chicago for his essay, "Antyllus, His Works and the Medicine of His Day." Honorable mention with a year's subscription to the *Bulletin* was awarded to Miss Daryl E. Beckman, College of Physicians and Surgeons of New York, for "Hippocratic Dietetics," and to Miss Jane F. Pascale, University of Chicago, for "The Dancing Mania. A Revaluation in the Light of 20th Century Knowledge."

Annual Meeting 1960

The Thirty-Third Annual Meeting will be held in Charleston, South Carolina, March 24-26, 1960.

Annual Meeting 1961

The Thirty-Fourth Annual Meeting will be held in Chicago at a time to be announced later.

JOHNS HOPKINS INSTITUTE OF THE HISTORY OF MEDICINE

As in past years, the Institute of the History of Medicine will admit a limited number of students for work leading to the degrees of Master of Arts and Doctor of Philosophy. Ordinarily no candidate for admission will be accepted whose record does not indicate some training in the medical (or kindred) sciences. The student, who will be enrolled in the Faculty of Philosophy of the Johns Hopkins University, must satisfy the requirements of either the Humanities or Social Sciences group of that Faculty. A Ph. D. candidate will have to show his ability to read French, German, and Latin. Written examinations of a comprehensive nature are required

of all candidates. Course work will be arranged to suit the requirements and interests of individual students who will also be expected to take courses offered by other departments in the Humanities and Social Sciences. Inquiries from individuals wishing to work for the M. A. or Ph. D. degree in the History of Medicine should be addressed to the Director of the Institute of the History of Medicine, School of Medicine, The Johns Hopkins University, 1900 East Monument Street, Baltimore 5, Maryland.

NATIONAL NEWS

Baltimore

The Johns Hopkins Medical History Club held its fifth meeting on June 2, 1959. Mr. Philip Reading, F. R. C. S., spoke on "History of Guy's Hospital, London."

The officers of the Club for the academic year 1959-60 are: Mark M. Ravitch, President, Palmer H. Futcher, Vice-president; Owsei Temkin, Secretary; Sanford V. Larkey, Delegate to the American Association for the History of Medicine.

Cleveland

Members of the American Association for the History of Medicine will be interested in the April, 1959, issue of the *Bulletin of the Cleveland Medical Library.* This number, welcoming the Association to Cleveland, carries several articles of historical interest, above all, one by Dr. Henry E. Fertig on "Our Heritage and Our Museum," and a report by Dr. Genevieve Miller on "Medico-Historical Activities."

Notable American Women, 1607-1950

Radcliffe College announces that it is sponsoring the preparation of a biographical dictionary of American women. To be titled *Notable American Women, 1607-1950,* it will contain sketches of approximately 1500 women from the colonial period onward and will comprise two or more volumes. The project is an outgrowth of the College's growing collection of manuscript and printed materials on the history of American women, the Womens' Archives. The articles in *Notable American Women* will be written by historians and other scholars and will, in general, be on the same scale as those in the *Dictionary of American Biography,* whose high scholarly standards the new work will strive to equal. (Virtually all the women in the *Dictionary* will be included in *Notable American Women,* though of course with fresh sketches.) The editor is Dr. Edward T. James, recently associate editor of Supplement Two of the *Dictionary of American Biography.* A committee of consultants has been appointed, headed by Arthur M. Schlesinger, Sr., of Harvard, but the editor solicits suggestions from scholars generally, particularly names of women who might be included and information about qualified contributors. He may be addressed at Radcliffe College, Cambridge 38, Massachusetts.

Pfizer Award

The History of Science Society has announced the establishment of a five hundred dollar annual award, to be given to an American scholar for a distinguished

contribution on a topic related to the History of Science. The prize, made possible by Chas. Pfizer & Co., Inc., is to be called the Pfizer Award. Selection of the Prize winner will be made each year by a rotating committee of three scholars, appointed by the Society's president with approval of its Council.

NEWS FROM ABROAD

Montreal

The manuscripts in the Osler Library of McGill University have been photo-filmed through the generosity of an anonymous benefactor, and the positive films are now available for inter-library loan. These include all items listed under "Manuscripts" in the index of the *Bibliotheca Osleriana*, 1929, except those of Osler's own writings, published, unpublished (his taboo), and (one) unpublishable.

BOOK REVIEWS

A. M. Lassek. *Human Dissection*, Its Drama and Struggle. Springfield, Illinois: Charles C Thomas, 1958. x + 310 pp. Ill. $6.50.

A study of the history of a technique involves necessarily the consideration of certain aspects of the field to which the technique has added new knowledge. Dr. Lassek's conscientious survey of the history of human dissection includes such background information. Hence this book is essentially a short history of anatomy from ancient times to the present. The text is a compilation of facts derived mostly from readily accessible writings on the history of anatomy, with each source acknowledged both in the text and in the bibliography; the whole arranged in a chronological sequence and subdivided under geographical headings. The presentation of the material occupies 20 chapters and is followed by a 21st chapter containing a summary and interpretation. A useful bibliography of 219 items is included and an excellent index completes the book.

Dr. Lassek begins his history of dissection by discussing the concepts of death and attitudes toward the dead body which developed among primitive peoples and in ancient civilizations. Although this section is brief and at times is marred by sweeping generalizations of debatable validity, the author does establish clearly the development of a fundamental dichotomy of thought which has hampered the study of human anatomy from ancient civilizations down to the present. On the one hand is the irrational emotional belief that the dead human body must be treated in some ritualistic way and protected from mutilation if the dead individual is to achieve an immortality or the society of the living is to be spared from affliction by some unknown evil spirit. On the other hand is man's rational curiosity concerning the structure of the human body and a recognition of the desirability of obtaining such knowledge, especially for the training of skilled physicians and surgeons. This conflict of emotion and reason, clearly evident in the highly developed culture of ancient Egypt, caused severe obstacles to be placed in the way of those desiring to dissect the human body, yet Greek and later societies gave recognition and respect for knowledge gained from such dissection, even though it was obtained through secret and illicit methods.

The problem of whether Galen ever dissected a human body is discussed, and the author concludes that he did not. Although some medical historians believe that Galen did dissect the human body, it seems probable that much of his knowledge was gained from dissecting the carcasses of lower animals. The recent discovery of a 4th Century A. D. fresco in a Roman catacomb, which some have interpreted as depicting an anatomy lesson, raises the question as to whether dissection of the human body was carried on during the "dark ages." Dr. Lassek does not discuss this interesting possibility.

The rise of human dissection during the European Renaissance is summarized competently, with principal emphasis on the work of Vesalius. This is followed

by narration of important events in the history of dissection from about 1650 to the present in Europe, Asia, and the United States. The section on anatomy in Asia is too brief and the references too old to be of much value in interpreting the current situation. The only mention of dissection in the Near and Middle East is a short paragraph on Iran. Thus the reader might gain the impression that the study of anatomy has remained static in Asia. Such an impression would be incorrect because great progress has been made, especially in the Near East since 1945, in such countries as Lebanon, Turkey, Iraq, Egypt-Syria, and Israel. The rise of resurrectionism in Great Britain is described in some detail for the purpose of explaining the passage of Warburton's Anatomy Act by Parliament in 1832, a law which put an end to grave-robbing on the British Isles.

Perhaps the most useful and interesting section of the book is the history of human dissection in the United States. This is not a complete history, however, since it is concerned only with the New England, Middle Atlantic, South Atlantic, and North Central States. Thus a considerable amount of material on the history of human dissection is untouched from such states as Kentucky, Tennessee, Missouri, Georgia, Louisiana, North and South Carolina, Alabama and Texas.

It is unfortunate that the author does not discuss more fully the history of the legal aspects of procuring human bodies for the purpose of dissection. The development of the "law of dead bodies," or the right for a "decent" burial of an unmutilated body by family or friends, is pertinent to an understanding of the present problem of a shortage of cadavers. The opinion derived from ancient common law that there is no property in a dead body presents an interesting problem to the courts, which has been resolved partially in some states by giving it a "quasi-property" interest. The anatomy laws which have been enacted in 44 states change the ancient common law only with respect to the bodies of a small group classed as unclaimed indigents. The phraseology of these laws indicates that they were framed primarily to stop grave-robbing rather than to advance the science of anatomy. As long as these laws stopped grave-robbing and, indirectly, also met the needs of anatomists, no problem existed. But in recent times the anatomical laws have been inadequate to meet the growing needs of the medical sciences, not only for anatomical study but also for pathological and clinical usage. The rise of transplantation of human tissues and organs has thrown an added strain upon these laws. Another source of difficulty is the increased amount of social welfare legislation, much of which nullifies the anatomical laws by abolishing the group of indigent dead. The value of Dr. Lassek's book would have been enhanced had he brought his historical material into focus more sharply with respect to these legal aspects of the disposal of the dead.

Although generally trustworthy as to the accuracy of his facts, the author has made a few statements which must be questioned. It is not likely that Julius Caesar, who was assassinated in 44 B. C., gave the order to burn the great library at Alexandria in the 1st Century A. D. (p. 50). The famous anatomical theatre at Padua was not built in 1446 (p. 81). This splendid building was erected in 1594. The elegant aula in which Vesalius conducted his anatomical demonstrations, as described by the author, never actually existed in its entirety (p. 97). The upper

portion of the theatre shown in the frontispiece of the *Fabrica* of 1543 was purely decorative; the lower portion may have depicted with some accuracy the actual appearance of the temporary structure at Padua in which Vesalius held his famous anatomical demonstrations. The author's list of works of literature which were inspired by the Burke and Hare incident (p. 173) omits an extremely interesting item: Dylan Thomas' *The Doctor and the Devils* (New York, New Directions, 1953). This work was intended to be a script for a motion picture concerned with the dealings of Burke and Hare with Dr. Robert Knox, but the film was never made. The date of the dissolution of the Worthington Medical College was 1839, not 1939 (p. 235).

The text is illustrated acceptably with 16 figures. Most of the figures will be familiar to experienced readers of medical history since they are taken from standard sources. Ten of the figures are taken from the writings of J. M. Ball (*The Sack'em-up Men* and *Andreas Vesalius*). The quality of the reproduction of the illustrations varies from excellent to poor, with most being just acceptable. Much detail in the fine engravings has been lost in the repeated copyings these prints have undergone.

The reader who is seeking a book on the history of anatomy which is both concise and moderately accurate will find this book of value.

S. R. Bruesch

Marie Boas. *Robert Boyle and Seventeenth-Century Chemistry.* New York: Cambridge University Press, 1958. viii + 240 pp. $5.50.

This important book undertakes to cast more light on the "old regime," before the "chemical revolution," in fact, to show that it was itself revolutionary. Introductory chapters on the early life of Boyle and the state of chemistry in the first half of the seventeenth century are succeeded by chapters on theories of matter, chemical composition, and on the relationship between the two. The book concludes with "A digression on air," and a discussion of the relationship, in Boyle's thought, between scientific method and chemical technique. The author concludes that "the amalgamation of chemistry and physics, and the development of rational mechanical theory in chemistry, amply indicate that seventeenth-century chemistry deserves a place in the seventeenth-century scientific revolution" (p. 231). As the principal ornament of this movement she disassociates Boyle from such phenomena, familiar to the historian of medicine, as "utilitarian iatrochemistry of mystical Helmontian dogma."

Professor Boas has invested a number of years in the study of Boyle, which justifies our expectation that the present work should represent a deeper insight into the subject than any heretofore to see the light. This book does satisfy that expectation. His published works have nowhere else been so thoroughly combed in modern times, to which material from manuscript sources has been added, particularly to cast additional light on his formative period. That period is of particular interest from the point of view of the history of medicine, for most of the chemists of the time were passionately devoted to the service of medicine, to which Boyle

seems relatively a decided contrast. Simply by giving greater attention to the matter, Professor Boas shows more comprehensibly that 1) Boyle was originally closer to the conventional medico-chemical authorities (e. g. Paracelsus, Beguin) than either Boyle or his earlier biographers admitted, 2) Boyle was not so much less interested in medicine as more interested in science in general, 3) the counteracting influences, which made Boyle something more than a medical chemist, were Francis Bacon and the (seventeenth century) atomic physicists.

Boyle's contribution to chemistry has often appeared to be largely negative, because of the prominence of his *Sceptical Chymist*. One of the greatest merits of the present work is its emphasis on his positive side, which the evidence of his other writings shows to have been very considerable. Bringing together bits and pieces of evidence scattered through the whole body of Boyle's work, Professor Boas shows convincingly that his physics and natural philosophy were at the source of his greatness as a chemist. Boyle devoted himself to making chemistry a part of natural philosophy through the application to it of the data and methodology of physics. In turning from preoccupation with the "elements" he was led to regard compounds more seriously as simple substances, and to devise tests for them.

These aspects of Boyle's work are recognizably akin to the activity of a modern chemist. It would not be surprising if to the medical chemists of his own time they did not seem especially pertinent, and it has often been remarked that Boyle's works altogether seem to have been of relatively little influence on his successors. The author, speaking of his "enormous scientific prestige," appears not to agree with this, but her study deals only briefly and generally with the question of his influence on his successors. Her reference to his influence through Newton is thought provoking, but remains undeveloped.

Professor Boas' conclusions are presented in a somewhat inconclusive way, but it is not difficult to suppose that this apparent defect is inherent in the subject. Well known is the diffuseness of Boyle's style and his haphazard method of publication, both formidable impediments to our understanding. These difficulties, and others springing from the peculiarities of seventeenth century chemical terminology, had to be courageously attacked in order to write the present book. Being neither a conventional biography nor a conventional study of the chemistry of a period, the book is not quite a substitute for either, but it should go far towards facilitating the writings of a comprehensive history of chemistry in the seventeenth century. One may wonder, however, if the author's tendency to find Boyle "dull," or to become impatient with him for not discovering more than he did, is not a violation of the credo of the historian of science, that the scientist of the past should be judged in the context of his own time.

This is a highly original work and demands the attention of anyone interested in the strange birth of that science we know as chemistry.

ROBERT P. MULTHAUF

HEINZ W. BUCHER. *Tissot und sein Traité des nerfs.* Zürich: Juris Verlag, 1958. 62 pp. 9.65 Swiss Francs. (Zürcher medizingeschichtliche Abhandlungen, Neue Reihe I.)

Two reasons determined the author of this first number in the new series of the Zurich studies (edited by E. H. Ackerknecht) to revive and to revitalize the eighteenth century physician, S. A. A. D. Tissot, who was the best known Swiss physician of his time. It is to him that we owe the first attempt to describe systematically, and in a sense to classify, and above all to interpret, a group of diseases known later, and still known today, as neurological diseases. Tissot also studied their etiology and found psychic factors emerging as frequent causes which cannot be ignored, and which relate the group to still earlier definitions of "nervous," hysterical, hypochondriacal, and similar conditions. Tissot, it is true, is better known for his pioneering role in public health and popular medical instruction ("avis au peuple"), and it seems that the author of this study sees here the main justification for claiming Tissot as a man of "enlightenment." He thereby restricts somewhat the meaning and scope of the term which has a much wider and universal connotation, unless used for no other purpose than to demarcate *chronologically* a well-defined era in the history of human thought. The author, after tracing Tissot's life and achievements, analyzes his *Traité des nerfs,* Tissot's only work of great scope which had been published. The comparative study of different editions and, above all, of Tissot's manuscripts, testifies to the author's historical sense and to the virtue of his method.

At a time when the problems implied in the nervous impulse and cerebral localization are in the foreground of neurological interests, one must be grateful for the revival of Tissot's early versions and pre-concepts, foreshadowing, though in terms of the eighteenth century, much of our present-day knowledge. The contemporary neurologist, all too frequently overstressing the *regional* approach, should welcome the rediscovery of an author of great standing who strove for an understanding of the activities of the nervous system by saving and re-affirming the role of *sympathies* or *remote* effects which had stood the test of medical experience since the days of antiquity.

WALTHER RIESE

JOHN DUFFY (Editor). The Rudolph Matas *History of Medicine in Louisiana,* Vol. 1. Published for the Rudolph Matas Trust Fund by Louisiana State University Press, 1958. xviii + 522 pp. Ill. $10.00.

It has often been said that the writing of a definitive history of medicine in the United States must await the publication of more state and local medical histories. The present volume represents a welcome contribution toward that desideratum.

The author, English-born John Duffy, professor of history at Louisiana State University, published in 1953 his first book on American medical history, *Epidemics in Colonial America,* one of many successful examples of the writing of medical history by a non-medical author. The volume before us represents many years of

labor on the part of Dr. Rudolph Matas, a vigorous and effective collector and compiler of historical material bearing on the development of medicine in Louisiana. At the age of ninety-five, this distingiushed New Orleans surgeon has not only turned over a wealth of data to Professor Duffy for editing and publishing but has provided the means for the accomplishment of the task.

The history of medicine in Louisiana begins with the year 1699, nearly a century later than the history of medicine in the English colony of Virginia. Louisiana was French, and for sixty-eight years its language, customs and medicine were French. Its contacts with the mother country were close, its destinies being controlled by a company somewhat like the London Company which managed the Virginia settlement in its first decades. French medicine was at its best, and the young Louisiana medical student, after beginning his studies at home, generally as an interne in the hospitals, was required to complete his training at Rochefort in France, an advantage not paralleled in the other colonies. Military garrisons of French soldiers were constantly maintained in the colony, with regimental surgeons and post hospitals. Medical education, medical practice, the hospitalization of both soldiers and civilians was at first provided for in these military establishments, although private medical practice prospered outside them also. Midwives enjoyed special recognition. The salary of the head midwife was paid out of public funds. Strenuous efforts were made to control malpractice, and the death penalty for certain infractions was on the books even though not strictly enforced. Varying from the other colonies in many respects, Louisiana offered its early settlers some experiences identical with theirs. There was, for instance, a starving time not unlike the period of suffering in the early days in Virginia, Massachusetts, and Canada. Indian medicine had some influence on medical practice in all the colonies. Louisiana apparently was no exception. For a time there as elsewhere medicinal plants were collected and cultivated with exuberant expectation. Epidemics took their toll with unpredictable frequency and African slaves introduced their special health problems.

Louisiana passed from France to Spain with little perceptible change—language, population, doctors remained dominantly French. The control over medical practice that had been exercised before was strengthened. Licensing, by the king's physician and examining boards, became more rigid. New arrivals were required to practice for six months in the city hospital without compensation. The subordination of the surgeon to the physician was emphasized in the regulations: "It is not the function of the surgeon to decide upon or employ any internal remedy." Surgeons were ordered to hold monthly meetings with a physician in attendance. The Charity Hospital became increasingly a community responsibility. The Royal Hospital was reserved for the exclusive care of military personnel. The Ursuline Nuns who had given sacrificial services to it in its early days finally withdrew, but the hospital remained under the domination of the Church. For many years Almonester was an important patron of the institution and for many years he and his descendants influenced its development.

A significant comparative scarcity of printed medical works existed in Louisiana in contradistinction to the other colonies. It is not surprising that even then town practice was more popular than rural practice. Epidemics of the previous period—smallpox and yellow fever,—continued to alarm, and to kill. Malaria was perennial. Dysentery and typhoid still took their toll. The first hesitant steps toward solving

the tremendous problems of public health were by now observable—the inspection of incoming vessels, quarantine, clean streets, and the location of graveyards away from inundation. Variolation, first atempted in 1787, because of ecclesiastical opposition was never employed in Louisiana to the same extent that it was in the colonies to the north.

The third and last section of the book carries forward the account from Jefferson's purchase of the territory in 1804 to the year 1825. Called by the author "The Transitional Period," it presents no sharp deviation from the medical conditions described in the Spanish and French periods, except in the rate of change due to the infiltration into the polyglot population of medical practitioners imbued with the rough and ready philosophy of the frontier. Their effect on medicine was to introduce those heroic methods of therapy which the more conservative earlier practitioners had avoided—the liberal use of phlebotomy, calomel and mercury. At this time medical education was obtained largely by apprenticeship although the more privileged students sought their medical training in the institutions of other colonies or of Europe. A few Negroes gained reputations as phlebotomists, and as nurses. Laws designed to improve standards of practice were enacted, but in general they failed to accomplish their purpose. Pestilence and plague continued, and uninfluenced by her economic prosperity New Orleans upheld her unsavory reputation as the plague spot of the country,—this in spite of the fact that sanitation was improved through new regulations and new agencies that required better food inspection, better methods of sewage disposal, and weekly mortality reports. The Charity Hospital continued to have its ups and downs. It records are rife with abuses no amount of legislative interference seemed able to correct. Its annual death rate of 35 per cent in 1822 was typical. The Medical Society of New Orleans, founded in 1817, straightway fell a prey to the jealousies and ethnic divisions that had so frequently hampered local medical progress.

Professor Duffy's story of medicine in one of the oldest and most colorful parts of our country is a valuable addition to our knowledge of early American medicine. We hope the promised second volume will be forthcoming soon.

WYNDHAM B. BLANTON

MAURICE DAVIDSON. *Memoirs of a Golden Age.* Oxford: Basil Blackwell, 1958. xvi + 140 pp. Ill. $3.75.

The "Golden Age" is the second half of the nineteenth century and the few succeeding years at Oxford University. Dr. Davidson's reminiscences cover in part medicine and surgery as it was taught as a pre-clinical science towards the closing years of the century when he was a student. He has put on record an account of the great teachers of the period, creating a picture which should stir the interest and imagination of scholars and students everywhere. The founding of the Oxford School of Medicine in its present form is comparatively recent, for Sir John Scott Burdon-Sanderson, superbly depicted in the "Spy" cartoon, was only appointed Waynflete Professor of Physiology in 1883. When Davidson knew him he had become the Regius Professor of Medicine, the predecessor of Osler in the same

chair. He seemed to typify the spirit of Oxford by his dignity and strength of character, "almost like a majestic being from another world." The teaching of medicine by Burdon-Sanderson was greatly influenced by another Oxford worthy, Sir Henry Acland, who built the great Museum in the mid-century and thus laid the foundations for the instruction of medical graduates. The head of the anatomy department was Professor Arthur Thomson, a brilliant teacher and, after 1905, a tower of strength to Sir William Osler. Francis Gotch followed Burdon-Sanderson in physiology, assisted by John Scott Haldane. A précis of his complete lectures was written on four blackboards, and every student copied it down *verbatim*. There were many other men of note, including those who gave preliminary instruction in clinical medicine at the Radcliffe Infirmary.

The college atmosphere was tuned to solid achievement, with an accent on human relations, an environment difficult to acquire in an age of mass production. Classes were small, the classic and humanitarian influences close at hand and teachers stood *in loco parentis* to students. The paramount need for a philosophy of life was ever present and the value of the heritage of the past was unquestioned. One feels that Davidson found in Oxford the priceless gift of a liberal education and some of that ethos he has transmitted to us in an inspirational manner.

Only a small part of this book deals with medicine; the rest is given over to memories of the heads of colleges, ecclesiastics, music, drama, traditions and ceremonies of the University. There is no index; most of the illustrations are "Spy" cartoons or photographs.

HENRY R. VIETS

JOHN M. GIBSON, *Soldier in White*, The Life of General George Miller Sternberg. Durham, N. C.: Duke University Press, 1958. 277 pp. Pt. $6.75.

Because we are still, historically speaking, a very young country with rich and productive energies directed towards present accomplishment and future goals; or perhaps because, self-conscious of our comparative youth we still suffer the adolescent pains of historical gaucheness, we often either completely ignore or cavalierly dismiss with the faint praise of a footnote many of the really important figures of our past. And in no field has this been more evident than in medical history.

When we evaluate the accomplishments of a Pasteur, Koch, Pavlov, or Sherrington perhaps simultaneously we underestimate our own, and in so doing blind ourselves to many of our own original and noteworthy contributions, and thereby relegate some truly significant accomplishments to the limbo of the undeservedly unremembered.

General George Miller Sternberg represents one of these undeservedly unremembered personalities. His name would evoke no reflex of remembrance in the mind of the medical student already familiar with the names Koch and Pasteur; and yet, as the Father of American Bacteriology, General Sternberg's name is eminently entitled to recognition.

Stimulated by the newly promulgated germ theory of disease, George Sternberg,

in the atmosphere of an Army Medical Service sterile of scientific curiosity, equipment, and encouragement, nevertheless produced an enviable corpus of achievement which eventually, and in his lifetime, earned him world recognition.

In 1881, and independent of Pasteur, Sternberg described the pneumococcus; he was moreover the first American to photograph, and among the very first to demonstrate, the newly discovered tubercle bacillus. Anticipating Metchnikoff by three years, he noted his belief that the white blood corpuscles were the long sought for agent responsible for the destruction of pathogenic bacteria. Sternberg's *Manual of Bacteriology*, published in 1892, was considered the outstanding work of that time in this field.

In scientific investigations of Yellow Fever and Malaria he disproved the frequently advanced theories of bacteriological etiology, and when Laveran discovered his Plasmodium, it was Sternberg who first demonstrated the organism on this continent (1886).

Sternberg's absorbing interest in Preventive Medicine and Public Health led him to the determinations of the thermal death point of various organisms and these, plus his auxiliary studies of germicidal agents, command his consideration as one of the co-founders (along with Koch) of scientific disinfection.

In contrast to our contemporary type of institutionalized research, opulently endowed with grants, scientific equipment, and general approbation, Dr. Sternberg worked as an individual. His only endowments were ingenious invention, scientific curiosity, and obstinate determination in the face of general public apathy. When his accomplishments earned for him the post of Surgeon-General, this far-sighted man established the Army Medical School—today our oldest institution of public health and preventive medicine—thus providing for those coming after the scientific milieu he himself was denied. Sternberg also recommended to Congress the formation of the Army Nurse Corps and the Army Dental Corps, and these were established in 1898.

As a medical soldier, General Sternberg was personally involved in three wars—the Civil, the Indian, and the Spanish-American. Brave beyond ordinary expectation, it was said of him that "he saw more active service on the battlefield during the Civil War and the Indian Campaign than any other medical officer of his time."

Thus Gibson's choice of subject is particularly suitable; not only because of Sternberg's sizeable and significant contribution to medicine but also because his great personal courage in war and his exciting individualistic exploits assure a fascination for the average reader that an equally important personage with a more prosaic background would lack.

Unfortunately the material is not new, having been available since 1920 in the biography of the General written by his wife. Less detailed than Mrs. Sternberg's biography, *Soldier in White* reads more fluidly in an acceptable semi-romantic treatment. In making this biography available to the general reading public John Gibson has nevertheless performed a valuable service. The professional treatment of the book, from a literary standpoint, will heartily recommend it to the non-medical reader or student interested in medical or general biography. For the physician, weary of the repetitious fascination of his daily round, *Soldier in White*

will afford a pleasant diversion and a brief but not unproductive excursion into medical history. For those wishing to know more of the subject, Mr. Gibson has provided an adequate, albeit admittedly incomplete, bibliography.

NORMAN SHAFTEL

LORD COHEN OF BIRKENHEAD. *Sherrington*, Physiologist, Philosopher, and Poet. (The Sherrington Lectures, IV) Springfield, Illinois: Charles C Thomas, 1958. xiv + 108 pp. Ill. $3.50.

Lord Cohen has provided us with an interesting and useful sketch of Charles Sherrington's life and career. He has divided his book into four sections: a biographical sketch, a survey of Sherrington's scientific contributions, a survey of Sherrington's non-scientific thought and writing and a bibliography. The biographical sketch though brief is interesting. Unfortunately it takes on the quality of an official biography and very little of the complexity of Sherrington's personality is permitted to show. The biographical chapter concludes, appropriately, with the phrase "He touched nothing which he did not adorn."

Lord Cohen introduces the chapter on Sherrington's scientific contributions with a commendable survey of the reflex theory as it developed up to the time when Sherrington began his studies. This survey will be of great value to the non-specialist reader. It is interesting to note that Sherrington held his most important predecessor, Pflüger, in some disdain. It has been suggested that he felt the same way toward his most important contemporary competitor, Pavlov. It is in this chapter that the truly monumental nature of Sherrington's life work becomes apparent. His mapping of the dermatomes, his discovery of the sensory nature of the muscle spindle, his discovery of reciprocal inhibition, his appreciation of the significance of the synapse, his elucidation of the general characteristics of reflex activity, his studies on decerebrate rigidity, his work on postural reflexes, and his studies of cerebral localization, enable us to agree that in the field of neurophysiology "he did bestride the narrow world like a Colossus."

Nor is it difficult to agree with Lord Cohen that in the field of philosophy "Sherrington's thinking cap was second-hand," or that his poetry "sometimes failed to gain the topmost peaks." All in all Lord Cohen's biography, by intention or not, serves to convince us that Sherrington was a scientific genius, and places strict limits to the myth that he was a universal genius. We may well be grateful for both of these aspects of the biography, and we may also hope for a longer and more detailed examination of the background and meaning of those scientific achievements which alone will make Sherrington immortal.

PAUL CRANEFIELD

THOMAS H. GRAINGER, JR. *A Guide to the History of Bacteriology.* New York: The Ronald Press Company, 1958. xi + 210 pp. $4.50. (*Chronica Botanica*: An international biological and agricultural series. No. 18.)

This book utilizes a new approach to the history of Bacteriology, or more accurately, the history of Microbiology. It is not limited to Medical Bacteriology, but includes sections on dairy, dental, food, industrial, insect, marine, sanitary, soil, sewage, warfare, and water bacteriology.

This guide was originally designed for a course on "History of Microbiology" offered at Lehigh University and has subsequently been used for this purpose in other universities. But it is equally valuable for research workers, librarians, bibliographers, and students of the history of bacteriology and science.

This work is not a chronological account of the history of bacteriology such as one finds in Bulloch's *The History of Bacteriology*, but a selective, annotated bibliography from which the scientist can select his own reading from original contributors and from various selected comprehensive reviews.

Part IV of the book presents a guide to the bibliographies of 90 selected bacteriologists arranged alphabetically from E. A. von Behring to Hans Zinsser.

The author has succeeded in producing an original new guide to reading in investigator.
Microbiology which will be of equal value to the student, the teacher, and the

DAVID T. SMITH

THE BULLETIN RECENTLY RECEIVED *

Thomas Neville Bonner. *The Kansas Doctor*, A Century of Pioneering. Lawrence: University of Kansas Press, 1959. xiv + 334 pp. Ill. $5.00.

J. Menzies Campbell. "Nitrous Oxide-Ether-Chloroform." Reprinted from: *The Dental Practitioner, 9*: 116-119, January, 1959.

Reinhold A. Dorwart. "Cattle Disease (Rinderpest?)—Prevention and Cure in Brandenburg, 1665-1732." Reprinted from: *Agricultural History, 33*: 79-85, 1959.

René Dubos. *Mirage of Health*, Utopias, Progress, and Biological Change. (World Perspectives, Volume Twenty-two). New York: Harper & Brothers Publishers, 1959. xv + 236 pp. $4.00.

Bentley Glass, Owsei Temkin, and William Straus, Jr. (Editors). *Forerunners of Darwin, 1745-1859*. Baltimore: The Johns Hopkins Press, 1959. 471 pp. Ill. $6.50.

M. D. Grmek. *On Ageing and Old Age*, Basic Problems and Historic Aspects of Gerontology and Geriatrics. (*Monographiae Biologicae*, 1958, Vol. V, No. 2). Den Haag: Uitgeverij Dr. W. Junk, 1958. 106 pp. Ill. 14 guilders.

William Harvey. *De Motu Locali Animalium 1627*. Edited, translated and introduced by Gweneth Whitteridge. New York: Cambridge University Press, 1959. xii + 163 pp. Front. $10.50.

Jose Joaquin Izquierdo. "Harvey en Mexico, hacia el tercer centenario de su muerte." Reprinted from: *Gaceta Medica de Mexico, 89*: 49-62, January, 1959.

Medical Department, United States Army. *Surgery in World War II: Neurosurgery*, Volume I. Ed. Glen Spurling and Barnes Woodhall. Washington, D. C.: Office of the Surgeon General, Department of the Army, 1958. xix + 466 pp. Ill. $5.00. [For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.]

Edward H. Richardson. *A Doctor Remembers*. New York: Vantage Press, 1959. 252 pp. Ill. $3.95.

Agustin Sanchez Martin. *El saber toco-ginecologico en la medicina española* de la primera mitad del siglo XVIII. Salamanca, 1958. (Publicaciones del Seminario de Historia de la Medicina, Universidad de Salamanca, Series A, T. II, N. 2, pp. 65-156).

Robert O. Steuer and J. B. de C. M. Saunders. *Ancient Egyptian and Cnidian Medicine*. The Relationship of their Aetiological Concepts of Disease. Berkeley: University of California Press, 1959. 90 pp. $3.00.

Carl J. Wiggers. *Reminiscences and Adventures in Circulation Research*. New York and London: Grune & Stratton, 1958. x + 404 pp. Ill. $9.75.

* The *Bulletin* reserves freedom of decision as to the publications to be listed in this section. Items received, other than those assigned for review, are ultimately incorporated into the collection of the Institute of the History of Medicine.

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